ORIGINAL ARTICLE

Incidence and risk factors for a second hip fracture in elderly women. The Study of Osteoporotic Fractures

R.D. Chapurlat · D.C. Bauer · M. Nevitt K. Stone · S.R. Cummings

Received: 7 March 2002 / Accepted: 3 September 2002 / Published online: 13 February 2003 © International Osteoporosis Foundation and National Osteoporosis Foundation 2003

Abstract Women with hip fracture have an increased risk of second hip fracture but other risk factors for a second hip fracture have not been established. We sought to determine the incidence and risk factors for second hip fracture, in a prospective cohort study of community-dwelling postmenopausal women over 65 years: the Study of Osteoporotic Fractures. From a cohort of 9,704 women, 632 women with a documented first hip fracture during the study were followed up until a second hip fracture or the end of follow-up. Clinical risk factors and bone mineral density were assessed at the beginning of the study. Fifty-three second hip fractures were validated by radiographs. Women with hip fracture had a 2.3% per year risk of second hip fracture. Women who walked for exercise at baseline were less likely to sustain a second hip fracture with a relative risk (RR) of 0.5 [0.3–0.9], as were those who had normal depth perception (RR = 0.5 [0.3-0.9]). Women who lost weight since age 25 years had an increased risk of second incident hip fracture (RR = 2.7[1.6–4.6]), as did those who had a low calcaneal bone mineral density (RR = 1.5 [1.1-2.0] per standard deviation decrease in bone mineral density). Current use of estrogen replacement therapy at baseline was protective (RR = 0.5 [0.3-0.9]) up to 2 years of follow-up. We conclude that community-dwelling women with a first hip fracture have a high risk of second hip fracture, and risk factors for this second fracture are similar to those of first hip fracture.

R.D. Chapurlat · D.C. Bauer · M. Nevitt · K. Stone S.R. Cummings

Prevention Sciences Group, University of California at San Francisco, California, USA

R.D. Chapurlat (🖂)

Department of Rheumatology and Bone Diseases, Pavillon F, Hospital E Herriot, 5 Place d'Arsonval, 69437 Lyon cedex 03, France E-mail: roland.chapurlat@laposte.net Keywords Estrogen · Osteoporosis · Risk factors · Second hip fracture

Introduction

Osteoporotic hip fractures are associated with an estimated 10–20% probability of death during the first year after fracture [1], and about a half the survivors suffer from disability [2]. Risk factors for first hip fracture have been well characterized [3, 4], and include previous fracture at any site, advanced age, low body weight and low bone mineral density (BMD). Several therapies are available to reduce fracture risk [5, 6, 7, 8], but only about 5% of women are treated properly after the occurrence of a first hip fracture [9]. Therefore, as the occurrence of any osteoporotic fracture is a strong predictor of subsequent fracture [3, 10, 11], many women who have sustained a hip fracture remain untreated and are at high risk for second hip fracture.

Our knowledge of the epidemiology of second hip fracture, however, is poorer than that of first hip fracture as fewer studies have addressed this issue [12, 13, 14 ,15, 16, 17, 18, 19, 20, 21]. In those studies, examining women, and sometimes men, annual incidences ranged from 2% to 10%, and risk factors were sometimes explored. Thus, neurologic diseases, falls, life in institution, dizziness, poor perceived health and osteomalacia were found to be associated with an increased risk of second hip fracture [16, 18, 19], whereas the predictive value of BMD and ultrasound remained unclear [19, 20]. The mean interval between first and second hip fracture was approximately 4 years, although it spanned from 1 to 13 years. Nevertheless, many potential risk factors for second hip fracture have not been collected in the literature, and the predictive value of BMD deserves to be clarified.

We therefore examined the incidence of and risk factors for a second hip fracture in elderly women in the Study of Osteoporotic Fractures, a population-based prospective cohort of Caucasian women, using risk factors collected at the baseline for the study.

Materials and methods

Participants

The Study of Osteoporotic Fractures (SOF) is a multicenter study of risk factors for fracture in 9,704 non-black women 65 years and older, recruited between 1986 and 1988 from population-based listings at four clinical centers in Portland, Oregon; Minneapolis, Minnesota; Baltimore, Maryland; and the Monongahela Valley, Pennsylvania. Details of the study methods have been published previously [22]. Black women were excluded because of their low incidence of hip fracture [23]. In addition, women unable to walk without assistance, and women with a bilateral hip replacement, were excluded.

This particular analysis was conducted in the 632 women who had a first hip fracture after inclusion in the study. Women who had a history of hip fracture before inclusion in the SOF were excluded to preserve the prospective collection of risk factors, which were measured before the first and the second hip fracture.

Measurements

During the baseline visit in 1986–8, we collected data about potential risk factors including reproductive histories, health habits, activity patterns and use of medications. Dietary calcium was assessed by a food-frequency questionnaire.

We measured weight, height (by stadiometer), and tested neuromuscular function as previously described [3]. We also assessed corrected visual acuity and contrast sensitivity, and we assessed depth perception using the Howard-Dohlman device, and scored it as the standard deviation of four trials [3]. Prevalence of vertebral fracture was assessed at baseline on spine radiographs using standard methods [24]. BMD of the calcaneus was measured using single photon absorptiometry (Osteoanalyzer, Siemens-Osteon, Wahiawa, HI) at baseline in all 632 women with subsequent first hip fracture. Total hip BMD was measured at the second visit in 488 of these women, using Hologic QDR 1000 scanners (Hologic, Waltham, MA). The coefficient of variation was of 1.2% for both sites.

Women were contacted every 4 months to determine their fracture status; 99% of these contacts were completed. All hip fractures were confirmed by central review radiographs. Pathologic fractures (including peri-prosthetic) and fractures secondary to extreme trauma were excluded.

Statistical analysis

We first compared baseline characteristics between women with one hip fracture and women with two hip fractures, using a t-test for normally distributed continuous variables with equal variances, a Mann-Whitney test for other continuous variables, or a chisquare test for dichotomous variables. We then calculated the incidence rate of second hip fractures among the 632 women who had a first incident hip fracture. We used a stratified proportional hazards analysis to identify independent risk factors of the second hip fracture. These risk factors were collected at the baseline for the study. Variables that had strong biological relevance or were associated with second hip fracture in univariate analyses (p < 0.1) were included in the multivariate model. The proportional hazard assumption was checked using graphical methods [25] and a specific goodness-of-fit test [26]. The proportionality assumption was met for all variables except baseline current estrogen use; therefore the final multivariate model was stratified on this variable. The proportionality assumption was met, however, for the first 2 years of follow-up for the variable baseline current estrogen use, so for this variable only we report adjusted estimates for 2 years of follow-up. We report hazard ratios as relative risks with 95% confidence intervals. All statistical tests were two-sided. All statistical analysis were conducted with STATA 6 software (Stata, College Station, TX).

Results

Baseline values of various variables of women with one incident hip fracture, women with two incident hip fractures and women with no incident hip fracture are displayed in Table 1. Among the 632 women who had an incident first hip fracture, 53 women had a second incident hip fracture not due to severe trauma-an incidence of 0.023 per person-year-during an average 3.7 years of follow-up. This incidence of second hip fracture was 4 times as great as that of a first hip fracture in the same cohort of ambulatory women. Second hip fracture occurred an average 2.3 years after the first one (maximum 6.8). The cumulative hazard did not plateau, for up to 6.8 years (Fig. 1). The second hip fracture occurred on the side opposite to the first one in most cases (93% women with a second hip fracture on the left side [26 of 28] had had their first one on the right side, and 96% women with a second hip fracture on the right side [24 of 25] had had their first one on the left side). Most second hip fractures were of the same type as the first one, with a stronger association for neck fracture (16/22, i.e., 72%) than for intertrochanteric fracture (18/16)31, i.e., 58%). The age of the women with a second incident hip fracture did not differ from that of the women with only one incident hip fracture, but they had lower body weight, lower calcaneal BMD, gained less weight since age 25 years, had more often an impaired depth perception, were less likely to take estrogen, to take calcium supplements, and to walk for exercise (Table 1). Among the 488 women who had a total hip BMD measurement, 69% of women who experienced a second hip fracture had a total hip T-score below 2.5.

In univariate analyses (Table 2) we identified six significant predictors of the risk of second hip fracture: low calcaneal BMD (total hip BMD was also a predictor of the risk of second hip fracture in the subset of 488 women who had this measurement made), protection by calcium supplements in the form of Tums (the protection was nearly significant for other types of calcium supplements), low body weight (i.e., <55 kg), low weight change since age 25 years (those who in fact lost weight) and protection by regular walks for exercise. Women taking any type of systemic estrogen at baseline were protected from a second incident hip fracture for up to 2 years after the first incident hip fracture, compared with women not taking estrogen. Age was not a significant predictor of the risk of second hip fracture, even though the relative risk of women in the three highest quartiles of age compared with those in the lowest quartile of age was around 2. The greatest age in the lowest quartile was 71 years. After separating

Table 1 Baseline characteristics of 632 women with one and two incident hip fractures, and of those with no incident hip fract	acture
--	--------

Characteristics	Women with only one incident hip fracture $(n = 579)$	Women with two incident hip fractures $(n=53)$	p value ^a	Women with no incident hip fracture $(n=9,072)$
Duration of follow-up (years)	3.8 ± 3.1	2.3 ± 1.9	0.002	na
Age (years)	75 ± 6	75 ± 5	0.79	71 ± 5
Weight (kg)	63.9 ± 11.5	60.6 ± 14.9	0.03	67 ± 12.5
Height (cm)	158 ± 6	156.5 ± 7	0.08	163 ± 6
Previous hyperthyroidism (%)	11.5	17	0.25	9
Currently taking estrogen (%)	13	9	0.04	16
Currently taking long-acting benzodiazepines (%)	11.6	16.7	0.27	11
Calcium intake from food per week (g)	4.6 ± 4.3	4.1 ± 4.3	0.24	5 ± 3
Current daily caffeine intake (g)	0.16 ± 0.14	0.18 ± 0.13	0.6	0.14 ± 0.14
Walking for exercise (%)	46	30	0.02	48
On feet $< 4 \text{ h/day}(\%)$	14	20	0.23	11
Weight gain since age 25 (kg)	8 ± 11.6	4.3 ± 11.2	0.02	11 ± 11
Height at age 25 years (cm)	163 ± 6	162 ± 6.5	0.22	163 ± 6
Pulse > 80 beats/min (%)	16	16.7	0.93	13
Impaired depth perception (%)	30	44	0.03	45
Ever taken Tums regularly (%) ^b	33	19	0.01	24
Prevalent vertebral fracture at baseline (%)	36	48	0.07	30
Calcaneal BMD (g/cm ²)	0.361 ± 0.095	0.316 ± 0.077	< 0.001	0.365 ± 0.084
Total hip BMD $(g/cm^2)^c$	0.674 ± 0.108	0.589 ± 0.111	< 0.001	0.638 ± 0.103

^aBaseline differences betweenwomen with one hip fracture and women with two hip fractures, usinga *t*-test for normally distributed continuous variables with equal variances, a Mann-Whitney test for other continuous variables, or a chi-square test for dichotomous variables Tums, and 28% had ever taken calcium supplements of other sorts. At baseline, 43% of women were currently taking calcium supplements of all sorts

^bSixty percent of women hadever taken calcium supplements of all sorts including Tums. Thirty-two percentof women had ever taken

^cTotal hip BMD was measured at the second visit, in a subset of 488 women with a first hip fracture, of whom 39 had subsequently a second hip fracture



Fig. 1 Cumulative hazard for second hip fracture

intertrochanteric and neck second hip fractures, we found that risk factors for intertrochanteric second hip fracture were essentially the same as those in the whole sample, whereas there was no significant predictor for neck second hip fracture, as we had a limited number of only 22 neck second hip fractures (data not shown).

In multivariate analyses stratified on current estrogen use, we found four independent predictors of the risk of second incident hip fracture (Table 3). Women with the lowest calcaneal BMD were at higher risk of second hip fracture compared with those with greater BMD. We

included calcaneal BMD in the final multivariate model. instead of total hip BMD, which is usually a better predictor of hip fracture, because this latter was measured in fewer women, and at the second visit rather that at baseline, thus allowing limited power for multivariate calculations. Women who walked for exercise were protected compared with the others. Women who had no impairment in their depth perception also had a lower risk of second incident hip fracture than the others. Conversely, women who had lost weight since age 25 years (women in the lowest quartile of weight change) were at higher risk of second hip fracture compared with those who gained weight. We did not include both body weight and weight change in the final model, whereas they were both significant predictors in univariate analyses, because of collinearity of these two variables (r=0.7). Weight change was chosen to be included in the model because it was more strongly associated with second hip fracture (Table 3). On the other hand, consumption of calcium supplements in the form of Tums was no longer a significant protector. The inclusion of calcium supplements other than Tums did not change the estimates. There was no association between the use of calcium supplements and that of estrogen (p=0.4). The inclusion of age, which was not a significant predictor in univariate analysis, did not alter results of this final multivariate model. During the first 2 years of follow-up after enrollment in the study, current estrogen use at baseline was associated with a lowered risk of second incident hip fracture, after adjustment for BMD,

Variable	Comparison	Relative risk (95% CI)	p value
Calcaneal BMD (g/cm ²)	Per standard deviation decrease	1.6 (1.2-2.2)	0.001
Total hip BMD (g/cm^2)	Per standard deviation decrease	2.1 (1.5–2.9)	< 0.001
Depth perception	Normal versus impaired	0.6 (0.4–1.1)	0.09
Visual acuity	Lowest quartile versus highest quartile	0.99(0.5-1.9)	0.99
Ever taken Tums regularly (32%)	All others without calcium supplement	0.6 (0.3–0.99)	0.04
Ever taken other calcium supplements $(28\%)^a$	All others without calcium supplement	0.6 (0.3–1.1)	0.09
Walking for exercise	All others	0.5 (0.3–0.9)	0.02
Weight (kg)	Lowest quartile versus all others	2.2 (1.3-3.8)	0.005
Weight gain since age 25 years (kg)	Lowest quartile versus all others	2.7 (1.6-4.6)	< 0.001
Weight at age 25 years (kg)	Lowest quartile versus highest quartile	1.0 (0.98–1.03)	0.85
Currently taking systemi cestrogen ^b	All others	0.2 (0.1–0.5)	< 0.001
Ever taken oral estrogen	All others	0.7(0.4-1.1)	0.13
Currently taking long-acting benzodiazepines	All others	1.5 (0.7–30)	0.28
Calcium intake from food per week	Lowest quintile versus highest quintile	1.7(0.6-5.1)	0.33
Still taking vitamin D	All others	0.7(0.2-2.4)	0.62
Alcohol (number of drinks per week)	Highest quartile versus others	1.2(0.7-2.2)	0.54
Drank alcohol in past 12 months	All others	1.5 (0.9–2.8)	0.15
Current daily caffeine intake (g)	Highest quartile versus lowest quartile	1.2(0.6-2.4)	0.57
Smoking (cigarette packs/year)	Highest quartile versus all others	0.8(0.4-1.5)	0.51
Height (cm)	Highest quartile versus all others	0.7 (0.3–1.3)	0.25
Height at age 25 years (cm)	Highest quartile versus lowest quartile	0.99(0.99-1.01)	0.35
Previous hyperthyroidism	All others	1.4 (0.7–3.0)	0.4
Still taking thyroid hormone	All others	1.9 (0.6–6.8)	0.31
Age (years)	Highest quartile versus lowest quartile	2,0(0.8-4.7)	0.13
Pulse rate lying down (beats/min)	Highest quartile versus lowest quartile	1.9 (0.8–4.7)	0.18
On feet < 4 h/day	All others	1.4(0.7-2.7)	0.34
Use arms to stand	All others	1.0 (0.4–2.6)	0.95
Education	Lowest level versus all others	1.0(0.97-1.2)	0.19
History of stroke	All others	0.6(0.08-4.1)	0.58
Osteoarthritis (self-report)	All others	1.1(0.6-2.1)	0.67
Cataract (self-report)	All others	0.7 (0.4–1.3)	0.31
Fainted in the last 12 months	All others	0.7 (0.2–3.0)	0.67
Health in last 12 months	Poor versus others	1.6 (0.2–15.4)	0.68
Fractured any bone after age 50 years	All others	1.2 (0.7–2.0)	0.54
Prevalent vertebral fracture at baseline	Fractured versus nonfractured	1.6 (0.9–2.7)	0.11
Mother's history of hip fracture	All others	1.6 (0.8–3.0)	0.17
Walking speed (m/s)	Lowest quartile versus highest quartile	1.2 (0.4–3.0)	0.73
Use of walking aids	All others	0.9 (0.3–2.3)	0.79
Difficulties standing up or walking up stairs	All others	0.6 (0.2–1.5)	0.3

^aup to 2 years of follow-up only

^bWhen data of women taking all types of calcium supplements were pooled and compared to women who had not taken any calcium supplements, a protective effect was observed which approached statistical significance (RR = 0.6 [0.6, 1.0])

use of Tums, impaired depth perception and weight change (Table 4). We were not able to determine the relationship between current estrogen use and second hip fracture after 2 years of follow-up, because the proportionality assumption of the Cox model was not met.

Discussion

Among older women in the SOF who had already had one incident hip fracture, we found a high incidence of second hip fracture (0.023 per person-year). We identified several independent risk factors for second incident hip fracture at the baseline for the study: low calcaneal BMD, impaired depth perception, low weight gain since age 25 years, and the absence of walking for exercise. Baseline current estrogen use was protective for up to 2 of follow-up.

The incidence rate of second incident hip fracture among women in the SOF who had already had a first incident hip fracture (0.023 per person-year) was 4 times as great as the incidence rate of first hip fracture in the same population [3]. This figure is consistent with the previous studies that examined incidence of second hip fracture, but in the lower range of incidence, probably because in other study populations many women were living in nursing homes, so they had a greater risk of fracture. We found that calcaneal BMD was a significant predictor of second hip fracture, whereas in previous analyses [19, 20], BMD was not significantly associated with the risk of second hip fracture. This difference may be due to the site of measurement and to a larger sample size. In one study [20], calcaneal ultrasound parameters and femoral neck BMD predicted second hip fracture, but not after adjustment for other risk factors. In contrast to an older study [16], we found no association between neurologic diseases and the occurrence of second

Table 3 Independent predictors of the risk of second incident hip fracture in multivariate Cox analysis^a, with stratification on current use of estrogen

Variable	Comparison	Relative risk (95% CI)	p value
Calcaneal BMD (g/cm ²) Walking for exercise Depth perception Weight gain since age 25 years (kg) Ever taken Tums regularly	Per standard deviation decrease All others Normal versus impaired Lowest quartile versus others All others without calcium supplement	$\begin{array}{c} 1.5 \ (1.1-1.96) \\ 0.5 \ (0.3-0.9) \\ 0.5 \ (0.3-0.9) \\ 1.9 \ (1.1-3.3) \\ 0.7(0.4-1.3) \end{array}$	$\begin{array}{c} 0.008 \\ 0.02 \\ 0.03 \\ 0.03 \\ 0.22 \end{array}$

^aThe multivariate model included calcaneal BMD, walking for exercise, depth perception, weight gainsince age 25 years and ever taken Tums regularly. Results were similar with inclusion of age in

Table 4 Predictors of the risk of second incident hip fracture in multivariate Cox analysis, with a maximum duration of follow-up of 2 years (n=625)

Variable	Comparison	Relative risk (95% CI)	p value
Calcaneal BMD (g/cm ²)	Per standard deviation increase	1.6 (1.0-2.6)	0.04
Walking for exercise	All others	0.7 (0.3–1.6)	0.35
Depth perception	Normal versus impaired	0.3 (0.1–0.8)	0.01
Weight gain since age 25 years (kg)	Lowest quartile versus others	2.6 (0.01-6.7)	0.046
Ever taken Tums regularly	All others without calcium supplement	0.4 (0.2–1.03)	0.06
Current systemic estrogen use	All others	0.2 (0.1–0.6)	0.002

hip fracture, which may result from differences in the study populations, because prevalence of those diseases was lower in the SOF. On the other hand, in the SOF risk factors for a fall increased the risk for second hip fracture, which is consistent with prior findings [16]. We could not confirm that osteomalacia conferred an increased risk of second hip fracture as we had no specific evaluation of this condition in the SOF.

We found that the second hip fracture occurred on the opposite side to the first one, which is consistent with previous observations. As most patients with hip fracture are treated using osteosynthesis or hip replacement, it is likely that these devices protect them from a new hip fracture on the same side if they fall again on this side. It is possible that risk factors for a second femoral neck hip fracture and a second trochanteric hip fracture differ somewhat, as do some risk factors for a first neck or trochanteric hip fracture [28], but we had no evidence for that, possibly owing to a lack of power. This might explain why second hip fractures were generally of the same type as the first one, because patients remained exposed to the same risk factors.

Weight and weight gain protected women from the occurrence of a second hip fracture, consistent with previous studies that found heavier women are somewhat protected from a first hip fracture [3, 29, 30, 31]. This protective effect of weight seems to be related to a greater BMD [31]. There is some evidence that body weight influences bone metabolism through weight loading and response of the skeleton to mechanical forces. It is also possible that adipose tissues play a role in absorption of energy of falls. Indeed, although the heaviest women generally have the greatest BMD, there is some evidence that adipose tissue is protective in itself

[32], maybe because reduced trochanteric soft tissue thickness is highly correlated with low body mass index. Weight loss and low body weight may also be indirect markers of poorer general health status. We did not ascertain whether weight loss was intentional or not. Furthermore, we could not determine whether current body weight or past weight change was more influential on the risk of second hip fracture, because of their high degree of correlation.

Calcium supplements conferred a protection against second hip fracture, but that was no longer significant in multivariate analysis. We cannot determine whether this was due to lack of precision of the estimate owing to limited power, or whether protection was mediated by other variables included in the model. Conversely, calcium intake in food was not associated with the risk of second hip fracture, as was found in the analysis of risk factors of the first hip fracture in the SOF [3]. As the use of calcium supplements was not associated with the use of other antiosteoporotic treatments available during the study period (e.g., estrogen replacement therapy), it is unlikely that the protective effect of calcium supplements had been confounded by other therapies.

Several risk factors we found in this study are of interest in the practical care of women who had a first hip fracture. Impairment of depth perception can be detected easily and often corrected. Although we cannot rule out that exercise may be a marker for health and functional status, walking regularly appeared to be protective. These results may support future clinical trials to assess the value of exercise and vision correction in women with a first hip fracture. BMD remained a significant predictor of the risk of second hip fracture even after adjustment for several variables. The magnitude of prediction was similar to that given for first fracture in a meta-analysis [33], i.e., a relative risk around 1.5 per standard deviation decrease in BMD.

It is of note that age was not a significant predictor of the risk of second hip fracture as opposed to the risk of first hip fracture [3], even though the relative risk of women in the three highest quartiles (>71 years of age) compared with those in the lowest quartile was around 2. There could be a threshold effect, albeit not significant, around the age of 71 years. Nevertheless, the addition of age in the multivariate models did not change the estimates. Some other factors predicting the risk of first hip fracture were also not significant predictors of the risk of second hip fracture, such as family history of hip fracture, smoking, and previous fractures other than hip. Thus, among older women who had a first hip fracture, these four potential risk factors of second hip fracture (age, family history of hip fracture, smoking, previous fracture other than hip) do not seem to sum to the overall risk of sustaining a second hip fracture, maybe because we have studied a subpopulation already at high risk, or because pathophysiology differs in some aspects.

In the subset of participants who had a total hip BMD measurement, most women who had a second hip fracture were in the osteoporosis range. Thus, one may infer that these women with the lowest hip BMD may benefit from bisphosphonate treatment to a larger extent than women who had experienced one hip fracture because they had a greater hip BMD, as it has been documented that bisphosphonate therapy reduces hip fracture only in women with the lowest *T*-scores. Our finding, however, is obtained in an observational study, so it deserves to be confirmed in a specifically designed randomized controlled trial.

Our study has several limitations. We examined only women who had a first incident hip fracture, and not those who had their first hip fracture before enrollment in the SOF. This design allowed us to collect risk factor information prospectively, before the first hip fracture. We were not able, however, to measure risk factors just before or after the first hip fracture, although functional status just before or after the first hip fracture might be a relevant risk factor. Rather, our perspective was of overall, long-term prevention of hip fracture. Several risk factors for a first hip fracture are also risk factors for a second hip fracture, so interventions targeting these risk factors will prevent a first hip fractures and lower the risk of a second fracture in those who have had one fracture, adding to the overall benefit of these measures. Our final model was stratified on the variable current estrogen use, because it did not meet the proportional hazards assumption. A time-dependent covariate analysis would have allowed estimation of the influence of estrogen use over the entire course of the study, but in the SOF, questions about treatments were not posed at all visits, so information concerning longitudinal use of estrogen use was not available. Therefore, being unable to incorporate all the changes in the variable "current estrogen use" that may have occurred during the study,

we chose to stratify the model on current estrogen use. Nevertheless, our results confirm previous findings in the SOF that estrogen therapy may reduce the risk of osteoporotic fracture only in current users but not in past users [34]. On the other hand, there were too few users of calcitonin and bisphosphonates to analyze. Risk factors for second hip fracture were similar to those of first hip fracture, suggesting that some of those risk factors might be relatively specific to the cohort, and might not be predictors in another cohort. Participants of the SOF were community-dwelling white women over the age of 65 years, so these findings are not generalizable to men, younger women, nursing homes residents, and women of other races. The women in the SOF may also have been healthier than the general population. We cannot rule out the possibility that some predictors, yielding smaller relative risks, may have been missed because of limited power.

In conclusion, we found a high incidence of second hip fracture 4 times as great as that of first hip fracture in a population-based prospective cohort of communitydwelling women. We identified several independent risk factors for the occurrence of the second hip fracture, such as impaired depth perception, low weight gain, absence of walking for exercise and low calcaneal BMD. Use of estrogen replacement therapy at baseline was protective.

Acknowledgements The Study of Osteoporotic Fractures has been funded by grants from the Public Health Service (1 RO1-AG05407, 1 RO1-AR35582, 5 RO1-AG05394, 1 RO1-AM35584, and 1 RO1-AR35583).

References

- Cummings SR, Black DM, Rubin SM. Lifetime risks of hip, collar, or vertebral fracture and coronary artery disease among white postmenopausal women. Arch Intern Med 1989;149: 2445–8.
- Beatriz JE, Perry HM III. Age-related osteoporosis. Clin Geriatr Med 1994;10:575–87.
- Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. N Engl J Med 1995;332:767–73.
- 4. Dargent-Molina P, Favier F, Grandjean H, et al. Fall related factors and risk of hip fracture: the EPIDOS prospective study. Lancet 1996;348:145–9.
- Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D₃ and calcium to prevent hip fractures in the elderly women. N Engl J Med 1992;327:1637–42.
- Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture women with existing vertebral fractures. Fracture Intervention Trial Research Group. Lancet 1996;348:1535–41.
- McClung M, Gueusens P, Miller PD, et al. Risedronate reduces hip fracture risk in elderly women with osteoporosis. N Engl J Med 2001;344:333–40.
- Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA 1999:282:637–45.
- Kamel HK, Hussain MS, Tariq S, et al. Failure to diagnose and treat osteoporosis in elderly patients hospitalized with hip fracture. Am J Med 2000;109:326–8.

- Black DM, Arden NK, Palermo L, et al. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. J Bone Miner Res 1999;14:821–8.
- Mallmin H, Ljunghall S, Persson I, et al. 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.
- Dretakis E, Kritsikis N, Economou K, Christodolou N. Bilateral non-contemporary fractures of the proximal femur. Acta Orthop Scand 1981;52:227–9.
- Melton LJ, Ilstrup DM, Beckenbaugh RD, Riggs BL. Hip fracture recurrence. A population-based study. Clin Orthop 1982;167:131–8.
- Boston DA. Bilateral fractures of the femoral neck. Injury 1983;14:207–10.
- Finsen V, Benum P. The second hip fracture. An epidemiologic study. Acta Orthop Scand 1986;57:431–3.
- Chiu KY, Pun WK, Luk KDK, Chow SP. Sequential fractures of both hips in elderly patients. A prospective study. J Trauma 1992;32:584–7.
- Schroder HM, Petersen KK, Erlansdsen M. Occurrence and incidence of the second hip fracture. Clin Orthop 1993;289:166– 9.
- Wolinsky FD, Fitzgerald JF. Subsequent hip fracture among older adults. Am J Public Health 1994;84:1316–8.
- Dretakis KE, Dretakis EK, Papakitsou EF, Psarakis S, Teriopoulos K. Possible predisposing factors for the second hip fracture. Calcif Tissue Int 1998;62:366–9.
- Stewart A, Walker LG, Porter RW, Reid DM, Primrose WR. Predicting a second hip fracture. J Clin Densitom 1999;2:363– 70.
- Dirschl DR, Piedrahita L, Henderson RC. Bone mineral density 6 years after a hip fracture: a prospective, longitudinal study. Bone 2000;26:95–8.
- 22. Cummings SR, Black DM, Nevitt MC, et al. Appendicular bone density and age predict hip fracture in women. JAMA 1990;263:665–8.

- 23. Farmer ME, White LR, Brody JA, Bailey DR. Race and sex differences in hip fracture incidence. Am J Public Health 1984;74:1374–80.
- Black DM, Palermo L, Nevitt MC, et al. Comparison of methods for defining prevalent vertebral deformities: the Study of Osteoporotic Fractures. J Bone Miner Res 1995;10:890–902.
- Kleinbaum DG. Survival analysis. Berlin Heidelberg New York: Springer, 1996.
- Grambsch PM, Therneau TM. Proportional hazards tests and diagnostic based on weighted residuals. Biometrika 1994;81:515–26.
- Schroder HM, Petersen KK, Erlandsen M. Occurrence and incidence of the second hip fracture. Clin Orthop 1993;289:166– 9.
- Fox KM, Cummings SR, Williams E, Stone K. Femoral neck and intertrochanteric fractures have different risk factors: a prospective study. Osteoporos Int 2000;11:1018–23.
- Grisso JA, Kelsey JL, Strom BL, et al. Risk factors for falls as a cause of hip fracture in women. N Engl J Med 1991;324:1326– 31.
- Farmer ME, Harris T, Madans JH, et al. Anthropometric indicators and hip fracture: the NHANES I epidemiologic follow-up study. J Am Geriatr Soc 1989;37:9–16.
- Chapurlat RD, Garnero P, Bréart G, et al. Serum estradiol and sex hormone binding globulin and the risk of hip fracture in elderly women: the EPIDOS study. J Bone Miner Res 2000;15:1835–41.
- Greenspan SL, Myers ER, Maitland LA, Resnick NM, Hayes WC. Fall severity and bone mineral density as risk factors for hip fractures in ambulatory elderly. JAMA 1994;271:128–33.
- Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996;312:1254–9.
- Cauley JA, Seeley DG, Ensrud K, et al. Estrogen replacement therapy and fractures in older women. Ann Intern Med 1995;122:9–16.