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Risk Factors for Hip Fracture in Men

Jeane Ann Grisso,[1] Jennifer L. Kelsey,[2] Linda A. O'Brien,[1] Carolyn G. Miles,[1] Stephen Sidney,[3] Greg Maislin,[1] Karin LaPann,[1] Deborah Moritz,[2] Beverly Peters,[3] and the Hip Fracture Study Group

To identify risk factors for hip fracture in men, the authors conducted a case-control study involving 20 hospitals in Philadelphia, Pennsylvania, and 14 hospitals in Kaiser Permanente Medical Care Program of northern California. The 356 enrolled men had been admitted with a radiologically confirmed first hip fracture. The 402 control men either were from the Philadelphia area or were members of Kaiser Permanente and were frequency matched to the cases by age and ZIP code or telephone exchange. Information on potential risk factors was obtained through personal interviews. Men in the lowest quintile of body mass had a greatly increased risk of hip fracture compared with men in the heaviest quintile (odds ratio (OR) 3.8, 95% confidence interval (CI) 2.3–6.4). Premorbid lower limb dysfunction was associated with increased risks for hip fracture (OR 3.4, 95% CI 2.1–5.4). Increased risks were also observed with the use of cimetidine (OR 2.5, 95% CI 1.4–4.6) and psychotropic drugs (OR 2.2, 95% CI 1.4–3.3). Smoking cigarettes or a pipe increased the risk of hip fracture, and this association was independent of body mass. Finally, previous physical activity was markedly protective. Factors thought to affect bone density as well as factors identified as risk factors for falls appear to be important determinants of the risk of hip fracture in men. Physical activity may be a particularly promising preventive measure for men. Additional studies of the use of cimetidine on osteoporosis and osteoporotic fractures are indicated. *Am J Epidemiol* 1997;145:786–93.

accidental falls; hip fractures; men; osteoporosis

Although men have lower age-specific incidence rates of hip fractures than women, hip fractures are common in men, affecting more than 1 percent of men 80 years of age and older each year (1, 2). Moreover, the mortality rate in men after hip fractures is nearly twice that of women (3). Although there have been few studies of risk factors for hip fracture in men, explanations for gender differences in hip fracture rates include differences in bone mass, absence of perimenopausal-associated bone loss, and possibly decreased rates of falls in men compared with women (4–9). The purpose of this case-control study is to identify risk factors for hip fracture in men.

MATERIALS AND METHODS

Study design and study subjects

Cases were men aged 45 years and older with a radiologically confirmed diagnosis of a first hip fracture who were admitted to one of 20 participating hospitals in Philadelphia or one of 14 hospitals in the Kaiser Permanente Medical Care Program of northern California (table 1). The study was conducted from 1991 through 1993. The study protocol was approved by the institutional review committees in each hospital in Pennsylvania and the Kaiser Permanente Medical Care Program in California. All study subjects gave written informed consent.

Cases were excluded whose hip fracture was pathological (metastatic cancer). An additional six cases who suffered major trauma (motor vehicle crash) were excluded from these analyses. The *International Classification of Diseases*, Ninth Revision, codes for classification of hip fracture were 820.0–820.9. Sixty percent of the fractures involved the femoral neck and the remaining 40 percent were trochanteric.

Of the potentially eligible cases, 356 (76 percent) participated, 62 (13 percent) refused to participate, 26 (6 percent) physicians refused on behalf of their patients, and 25 (5 percent) could not be traced after hospital discharge or were patients for whom a proxy respondent was needed but not available. Participants did not differ from nonparticipants in age, race, or geographic area of residence.

In Philadelphia, control subjects were randomly selected from lists of Medicare recipients generated by the Health Care Financing Administration for cases

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Abbreviations: CI, confidence interval; OR, odds ratio.

[1] Center for Clinical Epidemiology and Biostatistics, School of Medicine, University of Pennsylvania, Philadelphia, PA.
[2] Department of Health Research and Policy, School of Medicine, Stanford University, Stanford, CA.
[3] Kaiser Permanente Medical Care Program, Division of Research, Oakland, CA.
Reprint requests to Dr. Jeane Ann Grisso, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Blockley Hall, Room 920, 423 Guardian Drive, Philadelphia, PA 19104–6021.

TABLE 1. Characteristics of men with hip fractures and of controls from Pennsylvania and northern California, 1991–1993

Characteristic	Case patients (n = 356)		Controls (n = 402)	
	No.	%	No.	%
Age (years)				
45–64	47	13	46	11
65–74	84	24	95	24
75–84	119	33	143	36
≥85	106	30	118	29
Education (grade)				
None through 8th grade	72*	21	74*	19
9th through 12th grade	135	39	147	37
>High school	139	40	177	44
Race				
Caucasian	299	84	327	81
African-American	46	13	55	14
Other	11	3	20	5
Marital status				
Married	201*	57	271	67
Divorced	21	6	24	6
Separated	11	3	7	2
Widowed	98	27	79	20
Never married	24	7	21	5

*Subjects with missing data were excluded from individual analyses.

aged 65 years and older and through random digit dialing for cases 45–64 years of age (10). Community controls were frequency matched to cases by 10-year age group and either by ZIP code or telephone exchange. In northern California, control subjects were randomly selected from the lists of enrollees in the Kaiser Permanente Medical Care Program of northern California and frequency matched to cases by age and ZIP code.

Overall, of the 571 eligible controls, 402 (70 percent) were interviewed; 149 (24 percent) refused, three (0.5 percent) could not be contacted, and 25 (4.4 percent) required proxy respondents, when none was available. Although participants did not differ from nonparticipants in terms of age, there was a slightly higher response rate for African-American control subjects compared with Caucasian control subjects ($p = 0.03$).

Proxy respondents were interviewed, using a similar questionnaire, for subjects who were cognitively impaired or medically incapacitated (on ventilator support, comatose, or judged critically ill by a physician investigator). Cognitive impairment was defined as four or more errors on a modified version of the Short Portable Mental Status Questionnaire (11) on which a total of 145 hip fracture patients and 62 controls scored four or more errors. Proxy respondents were obtained for 125 cases and 37 controls.

Data collection

Interviews were conducted in person except for 11 cases and 22 control subjects who were interviewed by telephone. The proportion of interviews conducted with cases in hospital, at home, and in a nursing home were 26, 72, and 1 percent, respectively. Few cases were interviewed in a nursing home as the majority of those subjects required proxy interviews. The median duration of time from hip fracture occurrence to interview was 6.5 weeks.

Adjusted weight. The subjects' self-reported current height and weight were converted into meters and kilograms and used to calculate body mass index, which is the weight in kilograms divided by the square of the height in meters (12). The body mass index was divided into quintiles based on the distribution in controls. Height in centimeters was also included as a separate variable.

Lower limb function before the fracture. Cases and controls were asked whether they had needed assistance prior to fracture in performing four activities of daily living related to lower limb function: walking across a small room, getting out of a chair, walking outside on level ground, and walking up or down stairs. Assistance was defined as using an assistive device (cane, walker), a person's arm, or both. Scores were calculated as the number of tasks for which assistance was needed. Subjects totally confined to a bed or chair were given a score of 5. Physical impairment was determined separately by assessing the use of ambulatory aids such as a cane or walker.

Upper limb function before the fracture. Premorbid upper limb dysfunction was assessed by asking participants if they had had none, some, or a lot of difficulty with the following three tasks: extending arms above the shoulders, writing, and pushing or pulling an object. Participants reporting a lot of difficulty with one or more tasks were classified as very disabled, those reporting some difficulty (but not a lot of difficulty) with one or more tasks were classified as moderately disabled, and those reporting no difficulty with any of the tasks were classified as not disabled. Those who had reported being confined to bed or chair were classified separately as "confined."

Instrumental activities of daily living. Participants were asked if in the 6 months (before fracture) they were able to get around their own house, get around their own neighborhood, do light grocery shopping, or use public transportation. Those who reported not being able to carry out one or more tasks were compared with those who reported being able to conduct all of the tasks.

Chronic illnesses. Subjects were asked if a physician had diagnosed any of the following chronic ill-

nesses: Parkinson's disease, epilepsy, stroke, diabetes mellitus, coronary heart disease, kidney disease, or cancer.

Medications. Information was obtained on frequency, duration, and age of initiation of use of hormones and thiazide diuretic therapy. A specific question was included regarding prior use of steroid medications, which were uniformly reported as corticosteriods that were used for treatment of respiratory or rheumatologic conditions. We also included a specific question about prior use of cimetidine. Recent treatment (within the past month) with anxiolytic, hypnotic, antidepressant, and antipsychotic drugs was also queried.

Physical activity. A physical activity score was developed based on the reported average number of hours in the past year a subject had participated in each of the following activities: heavy outdoor work, outside household repairs or car repairs, heavy indoor work, and recreational exercise. The number of hours for each activity was summed and categorized into three levels as follows: 1) $\leq$60 hours per year; 2) 61–364 hours per year; and 3) >364 hours per year.

Hormone-related factors. Subjects were asked whether a physician had ever diagnosed cancer of the prostate and if so, were they treated with surgery or hormones. They were also asked whether they had ever unsuccessfully attempted to conceive a child for 12 months or longer and whether a physician had ever diagnosed a low sperm count or male infertility.

Alcohol and smoking. Smoking was defined as smoking at least one cigarette per day for 6 months or longer, smoking a pipe once a day for 6 months or longer, or one cigar per day for 6 months or longer. The average number of cigarettes smoked per day and duration of use were also determined. Current smoking was defined as smoking within the past year. Analyses were conducted separately for cigarette, cigar, and pipe smoking.

Alcohol consumption was assessed by asking participants about consumption in the past year and their usual frequency of use during their adult years. Alcohol consumption in the past year was classified as 1) none, 2) one to 13 drinks per week, and 3) $\geq$14 drinks per week. Self-respondents (not proxy respondents) were also asked whether they felt they had ever had a drinking problem.

Proxy questionnaire. Because of concern about potentially inaccurate reporting, the proxy respondent questionnaire excluded items on the duration of smoking. In addition, no information was obtained from proxy respondents regarding the subjects' past use of alcohol and whether they believed they had ever had a drinking problem.

Statistical analysis

Odds ratios and 95 percent confidence intervals were computed to estimate the relative risk, using conditional logistic regression analysis because of the large number of strata that resulted from matching (13). Matched sets were defined within state (California or Pennsylvania) by ZIP code or telephone prefix and age group. Initial analyses controlled for these design effects. Age was also included as a continuous variable to account for any residual confounding within the 10-year age strata. An initial multivariable model was estimated that included a set of variables identified as risk factors for hip fracture in previous studies of women. Variables were retained in the model if they were significant (using an alpha of 0.05) or if their removal changed the odds ratio of another variable by more than 15 percent (14, 15). Finally, each remaining variable in table 2 was added to the model one at a time. Variables were retained using the same criterion as described above.

We assessed whether there were differences between the odds ratios for self-respondents and for proxy respondents by obtaining separate estimates and comparing their magnitudes. The magnitude and direction of the odds ratios did not differ substantially, and the results from both proxy respondents and self-respondents are combined in the analyses presented here.

We also examined whether the odds ratios varied significantly by state. This was done by constructing state-specific multivariable models including the variables retained for the final multivariable model (listed in table 3) and formally comparing each variable by computing a Z statistic based on differences in the beta coefficients for each parameter from the state-specific models.

We assessed whether odds ratios varied with age. For each variable listed in table 3, we added an age by risk factor interaction term to the multivariable model in which age was dichotomized as <75 years and >75 years. No interactions with age were detected.

We conducted a preliminary evaluation of risk factors by hip fracture site (femoral neck vs. trochanter). Although no apparent differences emerged, the study size was limited to evaluate risk factors for this subgroup analysis.

RESULTS

The characteristics of the case and control subjects are shown in table 1. More than half of the case patients were 79 years old or older. Distributions of the case patients and the control subjects were similar with regard to age, years of education, race, and marital status.

The odds ratios for selected variables identified as possible risk factors or protective factors for hip fracture are shown in table 2. Men in the lowest quintile for body mass index (body mass index < 22.4) had an increased risk of hip fracture compared with men in the heaviest quintile (body mass index > 27.9) (odds ratio (OR) 3.8, 95 percent confidence interval (CI) 2.3–6.4). We analyzed the impact of height separately while adjusting for body mass index and found that height was independently associated with increased risk of hip fracture.

An increased risk of hip fracture was associated with lower limb dysfunction and the use of ambulatory aids before the hip fracture. In addition, the presence of upper limb dysfunction and difficulty with one or more instrumental activities of daily living were also associated with increased hip fracture risk. Several specific chronic illnesses were associated with increased risk (stroke, Parkinson's disease) as well as with having two or more chronic illnesses.

There was no overall association for the use of thiazide diuretic therapy despite rather common use (22 percent of controls) (OR 0.9, 95 percent CI 0.6–1.3). When we categorized thiazide diuretic use according to the duration of use, the OR for 5 or more years of use was 0.6 (95 percent CI 0.3–1.2). The use of cimetidine was associated with increased risk of hip fracture. Although no questions were included about a previous diagnosis of peptic ulcer disease, subjects were asked whether they had had previous gastric surgery. When subjects who responded affirmatively were excluded, the association of cimetidine use and hip fracture risk persisted (OR 1.8, 95 percent CI 1.1–3.0). Use of psychotropic drugs in the previous month was associated with increased risk of hip fracture.

Although gonadal function was not directly assessed, we evaluated several hormone-related factors. Reports of a physician diagnosis of male infertility or previous use of male hormone therapy were rare (2 percent of control subjects for each factor). Cases and controls did not differ in the proportion of subjects who reported unsuccessful attempts (of 12 months or longer) to conceive a child. Although the proportion of subjects who reported a previous diagnosis of cancer of the prostate was slightly higher in cases compared with controls, the differences were not statistically significant. Only three cases and two controls reported having received hormonal therapy for prostatic cancer.

Men were asked to report their frequency of physical activity in outdoor gardening work, outside repairs, heavy indoor chores, and recreational exercise. Markedly reduced risks of hip fracture were associated with participating in one or more of the activities for ≥7 hours per week (OR 0.2, 95 percent CI 0.1–0.3). When we excluded those with premorbid lower limb or upper limb dysfunction, the protective effect persisted (OR 0.6, 95 percent CI 0.4–0.8). We evaluated whether one type of activity was particularly protective. Odds ratios were <0.6 for each category of activity (gardening, outside repairs, heavy indoor chores, and recreational exercise). Of note, although the magnitude and direction of the associations did not differ by state, the level of physical activity was markedly greater in men from California compared with men from Pennsylvania. Control subjects from California reported participating in one or more of these activities for a median of 9.4 hours per week compared with a median of 2 hours per week reported by control subjects from Pennsylvania ($p = 0.0001$, Wilcoxon rank sum test).

Current cigarette smoking was associated with an increased risk of hip fracture among those who smoked one pack per day or more. Those who reported smoking pipes were also at increased risk compared with nonsmokers (OR 2.5, 95 percent CI 1.1–5.4). Those who reported smoking only cigars were not at increased risk. Past cigarette smokers were also at increased risk, and no reduction in risk was detected with increasing duration since quitting.

Current consumption of alcohol was not associated with increased risk of hip fracture despite a relatively high prevalence of heavy use (15 percent of controls reported consuming two or more drinks per day). We also had asked subjects whether their pattern of alcohol consumption had changed and for those individuals, how often they had consumed alcohol in the past. No association was detected for levels of past alcohol consumption and hip fracture risk. Finally, we asked self-respondents (not proxy respondents) if they felt that they had ever had a drinking problem. The results varied significantly by state ($p = 0.04$). In Pennsylvania, the risk of hip fracture was increased among those who reported a previous drinking problem (OR 3.5, 95 percent CI 1.4–8.7) whereas no association was detected in California (OR 1.1, 95 percent CI 0.6–2.1).

We constructed a multivariable conditional logistic regression model, retaining factors that were independent predictors of hip fracture and factors whose removal substantially altered the effect of one or more of the primary variables (table 3). The independent predictors included body mass index, history of stroke, lower limb dysfunction, use of cimetidine, use of psychotropic drugs, level of physical activity, and smoking. Of note, of the chronic illnesses assessed, only a prior history of stroke was independently associated with hip fracture risk after adjusting for lower limb dysfunction and physical activity level.

TABLE 2. Distribution of selected variables in men with hip fractures and in controls from Pennsylvania and northern California, 1991–1993*

Variable	Cases (n = 356)			Controls (n = 402)			Adjusted OR†,‡	95% CI†
	No.	%	Mean ± SE	No.	%	Mean ± SE		
Body mass index quintile§ (kg/m²)								
First (15.0–22.3)	141*	41		79*	20		3.8	2.3–6.4
Second (22.4–24.2)	78	23		78	20		2.2	1.3–3.7
Third (24.3–25.8)	43	13		81	20		1.0	0.6–1.9
Fourth (25.9–27.8)	43	13		81	20		1.0	0.5–1.8
Fifth (27.9–56.7)	37	10		82	20		Reference	
Height (cm)			176.4 ± 7.6				1.2	1.0–1.3¶
Presence of disease or disability								
Lower limb dysfunction#	203	57		94	23		4.5	3.0–6.6
Need for ambulatory aid**	174	49		85	21		3.7	2.5–5.5
Upper limb dysfunction								
Very disabled	97	27		40	10		4.3	2.5–7.2
Moderately disabled	88	25		101	25		1.4	0.95–2.1
Confined	18	5		6	1		3.8	1.2–12.0
No difficulty	153	43		255	63		Reference	
Instrumental activities of daily living (difficulty with one or more tasks)††	145	41		58	14		4.2	2.7–6.4
Stroke	84	24		36	9		3.2	1.9–5.3
Epilepsy	18	5		7	2		2.8	1.0–7.9
Parkinson's disease	21	6		4	1		7.9	2.2–28.2
No. of chronic illnesses‡‡								
2 – 5	58	14		35	9		2.5	1.5–4.3
1	118	33		139	35		1.3	0.9–1.8
0	180	51		228	57		Reference	
Medication history								
Use of thiazide diuretic therapy (years)								
≥5	18	6		37	10		0.6	0.3–1.2
1–4	29	9		38	10		1.0	0.5–1.8
0	262	85		311	81		Reference	
Use of cimetidine (ever vs. never)	39	11		26	6		2.5	1.4–4.6
Steroid therapy (ever vs. never)	22	6		12	3		1.9	0.9–4.2
Use of psychotropic drugs	90	26		71	18		2.2	1.4–3.3
Male hormone therapy (ever vs. never)	4	1		7	2		0.8	0.2–3.6

Table 2 continues

DISCUSSION

Although hip fractures cause substantial morbidity, disability, and mortality in men, hip fractures in men have received much less attention than in women (16, 17). It is thought that the lower age-specific incidence of hip fractures in men compared with women may be due to greater bone mass, the absence of a menopause-equivalent acceleration of bone loss, and a lower rate of falls in men (5, 8, 16, 17). Many of the results of this study of hip fracture in men are consistent with previous studies of women. Thinner men were at substantially greater risk for hip fracture than their heavier counterparts. The protection due to increased body mass in women has been postulated to be a result of increased adipose-based production of estrogen, greater gravitational forces on bone mass, and increased padding around the hips that may decrease the transmission of energy from the impact of the fall to the proximal femur (4, 18–20). Our results were similar to recent studies documenting that taller height was independent of body mass as a predictor of hip fracture, perhaps because individuals fell farther (9, 21, 22).

A number of chronic illnesses and measures of disability that have previously been reported as risk factors for falls were associated with increased risks of hip fracture in men (23, 24). Premorbid lower limb dysfunction, upper limb dysfunction, limitations in instrumental activities of daily living, and the previous use of an ambulatory aid were also associated with increased hip fracture risk.

TABLE 2. Continued

Variable	Cases (n = 356)			Controls (n = 402)			Adjusted OR†,‡	95% CI†
	No.	%	Mean ± SE	No.	%	Mean ± SE		
Hormone-related factors								
Cancer of the prostate	30	9		25	6		1.8	0.9–3.6
Physician diagnosis of male infertility	4	2		8	2		0.8	0.2–3.0
Never fathered a child despite trying for 12 months or longer*	14	6		19	5		1.2	0.6–2.6
Physical activity level§§								
High	66 *	19		147 *	37		0.2	0.1–0.3
Medium	94	26 *		125	32		0.3	0.2–0.5
Low	194	55		123	31		Reference	
Smoking and drinking								
Smoking pattern¶¶								
Current cigarette smoker ≥1 pack/day	51	14		23	6		3.2	1.7–6.0
Current cigarette smoker <1 pack/day	22*	6		18	5		1.6	0.7–3.5
Pipe	24	7		18	4		2.5	1.1–5.4
Cigar only	7	2		12	3		1.4	0.4–4.3
Former smoker	163	46		202	50		1.4	1.0–2.0
Nonsmoker	87	25		129	32		Reference	
Alcohol consumed during past year (drinks/week)								
≥14	52	15		63	16		0.7	0.4–1.2
1–13	148	41		202	50		0.7	0.5–0.9
0	156	44		137	34		Reference	

* Because of missing data, the numbers of men in some categories do not equal the total number. Percentages shown are based on actual observations.

† SE, standard error; OR, odds ratio; CI, confidence interval.

‡ Based on conditional logistic regression models, with adjustment for age category, Zip Code or telephone exchange, age as a continuous variable, and body mass index. Odds ratios of 1.0 were assigned to the reference groups.

§ Based on the distribution in the community controls.

¶ Increase in odds ratio per 6-cm increase in height.

Includes men who used a cane, walker, wheelchair, artificial leg, or leg brace or who were confined to bed.

** Defined by confinement to bed or by a requirement for ambulatory aids or help during the past 6 months for one or more of the following activities: walking across a room, walking outside on level ground, or going up or down stairs.

†† Defined by reporting difficulty during the past 6 months with one or more of the following activities: get around their own house, get around their own neighborhood, do light grocery shopping, or use public transportation.

‡‡ Expressed as a categorical variable and including the following five conditions: diabetes mellitus, coronary heart disease, epilepsy, kidney disease, and cancer.

§§ Physical activity based on the total number of hours in the past year reported doing heavy outdoor work, outside household repairs, heavy indoor work, and recreational exercise. The total number of hours were categorized as: 1) high, >364 hours in the past year; 2) medium, 61–364 hours in the past year; and 3) low, ≤60 hours in the past year.

¶¶ Pipe smoking defined as non-cigarette smoker who predominately smoked a pipe; occasional cigar use did not exclude individuals from that category. Cigar smokers were limited to individuals who smoked only cigars.

Although relatively little is known about the pathogenesis of osteoporosis in men, several factors were identified in this study that are thought to reduce bone density in men. Current heavy smoking of cigarettes and pipes was associated with increased hip fracture risk. Others have found that smoking may increase the risk of osteoporosis through decreasing body weight, earlier menopause in women, a decrease in testosterone levels in men, or a reduction in gastrointestinal absorption of calcium (4, 5, 8, 25). Although we did not assess testosterone levels or calcium absorption, the association of smoking and hip fracture risk in our sample of men was independent of body mass.

In our study, no association emerged between alcohol consumption and hip fracture risk despite a rather high proportion of both cases and controls reported consuming two or more drinks per day (15 and 16 percent of cases and controls, respectively). Although substantial evidence links chronic heavy alcohol consumption with osteoporosis in men, studies have not detected a consistent relation with moderate alcohol use and osteoporotic fractures (21, 26–30). It may be that continued alcohol use among the oldest old is a sign of health or the absence of serious illnesses.

Studies have shown an association between hypogonadism and osteoporosis in men (16, 32–34). Hy-

TABLE 3. Results of multivariable model of variables associated with hip fracture risk: comparing men with hip fractures with controls from Pennsylvania and northern California, 1991–1993

Variable	Adjusted OR*,†	95% CI*
Body mass index quintile‡		
First (15.0–22.3)	3.7	1.9–7.1
Second (22.4–24.2)	2.4	1.3–4.6
Third (24.3–25.8)	1.3	0.6–2.5
Fourth (25.9–27.8)	1.0	0.5–2.2
Fifth (27.9–56.7)	Reference	
Height (per 6 cm)	1.2	1.0–1.5
Lower limb dysfunction§	3.6	2.2–5.8
History of stroke (vs. none)	1.9	1.1+3.5
No. of chronic illnesses¶		
2 – 5	1.5	0.7–2.9
1	0.7	0.5–1.2
0	Reference	
Use of cimetidine (ever vs. never)	2.0	1.0–4.4
Use of psychotropic drugs	1.7	1.0–2.7
Level of physical activity#		
High	0.4	0.2–0.8
Medium	0.6	0.4–1.0
Low	Reference	
Smoking history		
Current smoker (≥1 packs/day)	3.3	1.5–7.1
Current smoker (<1 pack/day)	1.2	
Pipe	2.6	1.0–6.8
Cigar only	0.7	0.2–2.6
Former smokers	1.4	0.9–2.6
None	Reference	

* OR, odds ratio; CI, confidence interval.

† Based on conditional logistic regression models, with control for age category, Zip Code or telephone exchange, age as a continuous variable, and all other variables shown in the table. Odds ratios of 1.0 were assigned to the reference groups.

‡ Based on the distribution in the community controls.

§ Defined by confinement to bed or by a requirement for ambulatory aids or help during the past 6 months for one or more of the following activities: walking across a room, walking outside on level ground, or going up or down stairs.

¶ Expressed as a categorical variable and including the following five conditions: diabetes mellitus, coronary heart disease, epilepsy, kidney disease, and cancer.

Physical activity based on the total number of hours in the past year reported doing heavy outdoor work, outside household repairs, heavy indoor work, and recreational exercise. The total number of hours were categorized as: 1) high, >364 hours in the past year; 2) medium, 61–364 hours in the past year; and 3) low, ≤60 hours in the past year.

** Pipe smoking defined as non-cigarette smoker who predominately smoked a pipe; occasional cigar use did not exclude individuals from that category. Cigar smokers were limited to individuals who smoked only cigars.

pogonadism was not assessed in our study, and the self-reported prevalence rate of male infertility was too low (2 percent of controls) to have adequate power to evaluate. Of note, we did detect an association between the use of cimetidine and the risk of hip fracture. Chronic cimetidine use in men is associated with hyperestrogenic side effects, including gynecomastia. This may be linked to cimetidine-blocking androgen receptors or inhibition of estradiol 2-hydroxylation (34). Given that there has been little work evaluating chronic cimetidine use and bone metabolism in men, we believe these results should be interpreted with caution. Cimetidine use may also represent a marker of chronic peptic ulcer disease, which may be associated with osteoporosis.

The results of this study demonstrate marked protective effects of physical activity, regardless of whether the activity involves household repairs, gardening, or recreational activities. These results are consistent with studies involving small samples of men from Great Britain and Hong Kong (35, 36). To the extent possible, we evaluated whether the protective effect of physical activity was simply a function of the absence of disability. When we excluded those who reported previous limitations in lower or upper limb function, the protective effect remained. Physical activity may increase bone mass and decrease fall risk. Exercise programs have recently been shown to improve gait and reduce the risk of falling (37, 38).

Our findings are similar to those reported from a recent case-control study conducted at the Mayo Clinic based on medical record review (39). The authors reported that risks of hip fracture were increased with inactivity, increased height, thinness, as well as the number of chronic illnesses and that no effect was demonstrated for consumption of alcoholic beverages. It is important to note that the two study approaches have arrived at similar conclusions.

Several limitations of the present study should be mentioned. Because proxy respondents were not available for all men with severe cognitive impairment and because certain factors could not be assessed accurately in proxy interviews, the results of this study cannot be generally applied to men with severe cognitive impairment. It was not possible to validate the information reported by the subjects or by proxy respondents. In case-control studies, there is always a risk of recall bias. Finally, several potential risk factors were not assessed, such as dietary calcium, vitamin D intake, thyroid hormone therapy, and serum testosterone levels.

In this comprehensive study of risk factors for hip fracture in men, independent risk factors included conditions identified as risk factors for falls as well as risk factors thought to cause osteoporosis. The finding of an increased risk with cimetidine use is of concern given the prevalence of use. However, additional studies are needed to confirm or refute this association. Several preventive approaches are suggested based on the results of this study. Smoking cessation interventions, exercise programs, and limiting the use of psychotropic medications should be considered.

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The Hip Fracture Study Group includes the following individuals in Philadelphia, Pennsylvania: Dr. Alan Hibberd, Mercy Catholic Medical Center (Fitzgerald Mercy Division and Misericordia Division); Dr. Michael Clancy, Temple University Health Sciences Center; Dr. Jerome Cotler, Jefferson University Hospital; Dr. William DeLong, Cooper Hospital/University Medical Center; Dr. Malcolm Ecker, Chestnut Hill Hospital; Dr. Z. B. Friedenberg, Presbyterian-University of Pennsylvania Medical Center; Dr. Robert Good, Bryn Mawr Hospital; Dr. Charles Hummer, Crozier-Chester Medical Center; Dr. Charles Hummer, Sacred Heart Hospital; Dr. William Markman, Jeanes Hospital (Fox Chase Cancer Center); Dr. Pekka Mooar, Medical College of Pennsylvania; Dr. Herbert Stein, Frankford Hospital; Dr. Herbert Stein, Frankford-Torresdale Division; Dr. Milton Wohl, Albert Einstein Medical Center; Dr. Dennis Zaslow, St. Joseph Hospital.

REFERENCES

1. Jacobsen SJ, Goldberg J, Miles TP, et al. Hip fracture incidence among the old and very old: a population-based study of 745,435 cases. Am J Public Health 1994;80:871–3.
2. Lu-Yao GL, Baron JA, Barrett JA, et al. Treatment and survival among elderly Americans with hip fractures: a population-based study. Am J Public Health 1994;84:1287–91.
3. Jacobsen SJ, Goldberg J, Miles TP, et al. Race and sex difference in mortality following fracture of the hip. Am J Public Health 1992;82:1147–50.
4. Cummings SR, Kelsey JL, Nevitt MC, et al. Epidemiology of osteoporosis and osteoporotic fractures. Epidemiol Rev 1985;7:178–208.
5. Jackson JA, Kleerekoper M. Osteoporosis in men: diagnosis, pathophysiology, and prevention. Medicine 1990;69:137–52.
6. Scane AC, Francis R. Risk factors for osteoporosis in men. Clin Endocrinol 1993;38:15–16.
7. Grisso JA, Chiu GY, Maislin G, et al. Risk factors for hip fractures in men: a preliminary study. J Bone Min Res 1991;6:865–8.
8. Orwoll ES, Klein RF. Osteoporosis in men. Endocrine Rev 1995;16:87–116.
9. Hemenway D, Azrael DR, Rimm EB, et al. Risk factors for hip fracture in US men aged 40 through 75 years. Am J Public Health 1994;84:1843–5.
10. Hatten J. Medicare's common denominator: the covered population. Health Care Financ Rev 1980:53–64.
11. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J Am Geriatr Soc 1975;22:433–41.
12. Garrow JS, Webster J. Quetelet's index (W/H2) as a measure of fatness. Int J Obesity 1985;9:147–53.
13. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic research: principles and quantitative methods. Belmont, CA: Wadsworth, Inc., 1982.
14. Gail MH, Lubin JH, Rubinstein LV. Likelihood calculations for matched case-control studies and survival studies with tied death times. Biometrika 1981;68:703–7.
15. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. Am J Epidemiol 1989;129:125–37.
16. Seeman E. Osteoporosis in men: epidemiology, pathophysiology, and treatment possibilities. Am J Med 1993;95:22S-8S.
17. Niewoehner, CB. Osteoporosis in men. Is it more common than we think? Postgrad Med 1993;93:59–70.
18. Cummings SR, Nevitt MC. A hypothesis: the causes of hip fractures. J Gerontol Med Sci 1989;44:M107–11.
19. Farmer ME, Harris T, Madans JH, et al. Anthropometric indicators and hip fracture: the NHANES 1 Epidemiologic Followup Study. J Am Geriatr Soc 1989;37:9–16.
20. Lauritzen JB, Askegaard V. Protection against hip fractures by energy absorption. Dan Med Bull 1992;39:91–3.
21. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. N Engl J Med 1995;332:767–73.
22. Greenspan SL, Myers ER, Maitland LA, et al. Fall severity and bone mineral density as risk factors for hip fracture in ambulatory elderly. JAMA 1994;271:128–33.
23. Grisso JA, Kelsey JL, Strom BL, et al. Risk factors for falls are important determinants of hip fracture in women. N Engl J Med 1991;324:1326–31.
24. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988;319:170–1.
25. Baron JA, La Vecchia C, Levi F. The antiestrogenic effect of cigarette smoking in women. Am J Obstet Gynecol 1990;162:502–14.
26. Seeman E, Melton LJ III, O'Fallon WM, et al. Risk factors for spinal osteoporosis in men. Am J Med 1983;75:977–83.
27. Lindholm J, Steiniche T, Rasmussen E, et al. Bone disorder in men with chronic alcoholism: a reversible disease? J Clin Endocrinol Metab 1991;73:118–24.
28. De Vernejoul MC, Bielakoff J, Herve M, et al. Evidence for defective osteoblastic function: a role for alcohol and tobacco consumption in osteoporosis in middle-aged men. Clin Orthopaed Rel Res 1983;179:107–15.
29. Cumming RG, Klineberg RJ. Case-control study of risk factors for hip fractures in the elderly. Am J Epidemiol 1994;139:493–503.
30. Felson DT, Kiel DP, Anderson JJ, et al. Alcohol consumption and hip fractures: the Framingham Study. Am J Epidemiol 1988;128:1102–10.
31. Finkelstein JS, Klibanski A, Neer RM, et al. Osteoporosis in men with idiopathic hypogonadotropic hypogonadism. Ann Intern Med 1987;106:354–61.
32. Stanley HL, Schmitt BP, Poses RM, et al. Does hypogonadism contribute to the occurrence of a minimal trauma hip fracture in elderly men? J Am Geriatr Soc 1991;39:766–71.
33. Jackson JA, Riggs MW, Spiekerman AM. Testosterone deficiency as a risk factor for hip fractures in men: a case-control study. Am J Med Sci 1992;304:4–8.
34. Galbraith RA, Michnovicz JJ. The effects of cimetidine on the oxidative metabolism of estradiol. N Engl J Med 1989;321:269–74.
35. Lau E, Donnan S, Barker DJP, et al. Physical activity and calcium intake in fracture of the proximal femur in Hong Kong. BMJ 1988;297:1441–3.
36. Cooper C, Barker DJ, Wickham C. Physical activity, muscle strength, and calcium intake in fracture of the proximal femur in Britain. BMJ 1988;297:1443–6.
37. Fiatarone MA, O'Neill EF, Ryan ND, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med 1994;330:1769–75.
38. Province MA, Hadley EC, Hornbrook MC, et al. The effects of exercise on falls in elderly patients. JAMA 1995;273:1341–7.
39. Poor G, Atkinson EJ, O'Fallon MW, et al. Predictors of hip fractures in elderly men. J Bone Min Res 1995;10:1900–7.