

Second Hip Fracture in Older Men and Women

The Framingham Study

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Background: Older persons with hip fractures remain at increased risk of subsequent hip fractures. However, little is known about the frequency and characteristics of persons who sustain a second hip fracture.

Methods: Participants included 481 members of the Framingham Heart Study who sustained an initial hip fracture between April 1952 and December 31, 2003. Participants were followed up until a second hip fracture, death, dropout, or study completion. Age, sex, falls, stroke, dementia, residence, recent weight change, body mass index, and functional status were considered potential predictors of a second hip fracture.

Results: During a median of 4.2 years of follow-up, 71 subjects (14.8%) experienced a second hip fracture. Following a first hip fracture, 2.5% of subjects experienced a second hip fracture within 1 year, and 8.2% of subjects (9.7% of women) experienced a second hip fracture within 5 years. One-year mortality following an ini-

tial hip fracture was 15.9% compared with 1-year mortality following a second hip fracture of 24.1%. The risk of a second hip fracture increased with age (hazard ratio [HR] per 5-year increase in age, 1.5; 95% confidence interval [CI], 1.1-1.8) and with high functional status (HR compared with moderate functional status, 2.7; 95% CI, 1.1-6.9). There was a statistically nonsignificant association between low functional status and the risk of second hip fracture (HR compared with moderate functional status, 3.7; 95% CI, 0.9-14.8).

Conclusions: Among survivors of an initial hip fracture, the incidence of a second hip fracture is substantial. Older age and functional status may be important predictors of a second hip fracture. There seems to be adequate time between the first and second hip fractures for interventions that may reduce second hip fractures.

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EACH YEAR, MORE THAN 300 000 hip fractures occur in the United States alone.¹ These fractures are known to increase morbidity, mortality, and nursing home admissions, with associated high costs.² Although there are few proven therapies to reduce secondary fractures among persons with a hip fracture, clinical guidelines recommend treatment of osteoporosis for all women with a vertebral or hip fracture.³ Despite these recommendations, few clinicians initiate osteoporotic therapy following a hip fracture, particularly in elderly persons.^{4,5}

It is not surprising that many persons who fracture a hip will sustain a second hip fracture. In fact, the frequency of a second hip fracture among persons with an initial hip fracture is estimated at between 2% and 11%.⁶⁻¹⁵ The mean time between the first and second hip fractures is 2.0 to 4.3 years, with many of the second fractures occurring during the first year of follow-up.^{8,9,11,12,14,15}

Less is known about risk factors for a second hip fracture. Falls, dementia, advancing age, loss of weight or height, maternal history, use of benzodiazepines, and poor visual acuity are associated with an increased risk of initial hip fracture in postmenopausal women.^{16,17} However, risk factors for a second hip fracture may differ from these previously identified factors because persons with a second hip fracture must be able to survive the stress of an initial hip fracture to be at risk for a second hip fracture. Few studies have addressed risk factors for a second hip fracture separately. Dementia, Parkinson disease, history of falls, osteomalacia, and institutionalization are associated with an increased risk of second hip fracture in men and women.^{8,11,13,15} Weight loss and poor perceived health are associated with a second hip fracture in postmenopausal women, while estrogen use, regular walking, and normal visual acuity were protective of a second hip fracture in the same group.¹⁰

STUDY POPULATION

This study included members of the original Framingham Heart Study, a prospective cohort that enrolled 5209 residents of Framingham, Massachusetts, between the ages 28 and 62 years, with the goal of studying cardiovascular risk factors.¹⁸ Since 1948, these individuals have been examined every 2 years. Follow-up is complete for 99.0% of participants. Subjects include all members with an initial hip fracture between April 1952 and December 31, 2003. Subjects were followed up from the time of their initial hip fracture until the primary outcome of a second hip fracture or until death, dropout, or December 31, 2003.

HIP FRACTURE ASCERTAINMENT

Hip fractures were ascertained by a review of hospitalization and death records and by direct questioning at later examinations. Periprosthetic fractures (n=1) were excluded. Traumatic fractures (work injury [n=1], motor vehicle crash [n=3], and injury on stairs or ladder [n=5]) were included. One subject experienced simultaneous bilateral hip fractures. This individual was analyzed as having a first hip fracture only.

DATA COLLECTION

Because our goal was to identify clinical characteristics at the time of the initial hip fracture that might be helpful in predicting a second hip fracture, baseline characteristics were assessed at the study examination closest to and preceding the initial hip fracture. For example, if a participant experienced a first hip fracture between examinations conducted in 1978 and 1980, baseline characteristics were collected from the examination in 1978. We evaluated sex, falls, stroke, baseline age, dementia, 4-year weight change, functional status, nursing home residence, and body mass index (BMI) with respect to the risk of second hip fracture. Weight without shoes was measured to the nearest pound. Four-year weight change was calculated as the difference in weight measured at the baseline examination and 4 years earlier. Height was measured using a stadiometer to the nearest one-fourth inch. Stroke was determined by a panel of neurologists using standardized criteria.¹⁹ Dementia of all subtypes was assessed by neuropsychological testing and neurological examination using methods previously described.¹⁹ Residence and history of falls within the past year were obtained from standardized questionnaires.

Functional status was measured 2 ways. First, the modified Katz Activities of Daily Living Scale measured the ability to eat, dress, bathe, and transfer independently. Second, the 3-item Rosow-Breslau Scale measured the ability to perform heavy housework, climb a flight of stairs, and walk one-half to 1 mile independently. Because most participants were independent in their activities of daily living (**Table 1**), a combined functional scale was created. High functional status was defined as the ability to perform all Rosow-Breslau Scale and modified Katz Activities of Daily Living Scale items independently. Moderate functional status designated independence in all modified Katz Activities of Daily Living Scale items but an inability to perform at least 1 of the Rosow-Breslau Scale items independently. Low functional status indicated dependence in at least 1 item of both the modified Katz Activities of Daily Living Scale and the Rosow-Breslau Scale. Although this combined scale has not been validated in the literature, both component scales are commonly used for research purposes and have been individually validated.^{20,21}

Table 1. Baseline Characteristics of Persons With an Initial Hip Fracture According to Whether They Experienced a Second Hip Fracture

Characteristic	No. of Participants	Second Hip Fracture ^a	
		Yes (n = 71)	No (n = 410)
Age, y	481	77.2 ± 10.2	80.3 ± 9.5
Female sex	481	90.1	78.5
Weight, lb	262	128.4 ± 24.1	136.4 ± 27.0
Height, in	481	62.1 ± 2.9	62.3 ± 3.7
Body mass index ^b	262	23.4 ± 3.7	24.5 ± 4.3
Estrogen use ^c	386	1.6	0.9
Tobacco use	480		
Never		48.6	43.7
Former		32.9	38.3
Current		18.6	18.1
4-y Weight change, lb	235	-1.7 ± 9.7	-6.0 ± 12.7
Stroke	467	5.8	13.6
Dementia ^d	344	11.5	14.4
Nursing home residence ^d	254	4.8	11.3
Prior falls ^d	207	33.3	40.4
No. of modified Katz Activities of Daily Living Scale items performed independently ^d	264		
0-1		4.8	8.1
2		7.1	5.4
3		2.4	2.3
4		85.7	84.2
No. of Rosow-Breslau Scale items performed independently ^d	235		
0-1		25.0	48.7
2		16.7	24.1
3		58.3	27.1
Functional status ^e	214		
High		61.8	30.0
Moderate		23.5	53.9
Low		14.7	16.1

SI conversion factor: To convert pounds to kilograms, multiply by 0.45.

^aData are given as mean ± SD or as percentages.

^bCalculated as weight in kilograms divided by height in meters squared.

^cBecause the prevalence of estrogen use among women experiencing at least 1 hip fracture was low (1.1%) in this cohort, women with missing estrogen data (n = 154) were considered nonusers of estrogen.

^dInformation on these predictors was not available throughout the study (dementia, first available in 1974; functional status, first available in 1975; residence, first available in 1980; and falls, first available in 1982).

^eHigh functional status was defined as subjects able to independently perform the 4-item Activities of Daily Living (ADLs) Scale (eating, bathing, dressing, transferring) plus the 3-item Rosow-Breslau Scale (walk 0.5-1 mile, climb a flight of stairs, and perform heavy housework); moderate functional status, as subjects able to perform the 4-item ADLs Scale independently but unable to perform all 3 items from the Rosow-Breslau Scale independently; low functional status, as subjects unable to perform at least 1 item of both the ADLs Scale and the Rosow-Breslau Scale independently.

Most existing studies of a second hip fracture include modest numbers of subjects with short follow-up and may underestimate the incidence of second hip fractures. It is important to fully describe the duration between first and second hip fractures because this has clinical implications on treatment and prevention efforts. Therefore, this study contributes to the existing literature by describing the timing, incidence, risk factors, and mortality associated with second hip fractures using a large population-based cohort with long-term follow-up.

STATISTICAL ANALYSIS

A cumulative incidence estimate, accounting for variable follow-up and competing risk of death, was used to describe the time to second hip fracture for men and women separately (**Figure**).²² A log-rank test was used to compare mortality rates following a first hip fracture in men and women.

Age- and sex-adjusted Cox proportional hazards regression analysis was performed for each characteristic separately. Variables associated with a second hip fracture in the age- and sex-adjusted analyses at a significance level of $P < .10$, as well as clinically important predictors (sex), were included in the multivariate models. Because an increased incidence of fall-related injuries has been observed in very high- and very low-functioning persons, moderate functional status was designated as the reference group in these models.²³ Given that many predictors were unavailable until later examinations, the final model contained only 178 subjects (37.0% of the cohort), 30 of whom experienced a second hip fracture.

A sensitivity analysis was performed using multiple imputation to assign values to missing covariates (MI and MIANALYZE procedures; SAS Institute, Cary, North Carolina). Given the observed data, these imputations assume the mechanisms that lead to missing data do not depend on unobserved data. All analyses were performed using SAS version 9.1 (SAS Institute).

RESULTS

Study participants include 481 members (95 men and 386 women) of the Framingham Heart Study with a first hip fracture. The incidence of first hip fractures among the entire Framingham cohort was 0.28 cases per 100 person-years. The median age at first fracture was 81 years and ranged from 45 to 99 years.

During a median of 4.2 years (interquartile range, 1.4-8.9 years) of follow-up, 14.8% of subjects (7 men and 64 women) experienced a second hip fracture. Ninety-two percent of second hip fractures occurred on the hip opposite the initial fracture. Among persons with a first hip fracture, the incidence of second hip fractures was 2.3 cases per 100 person-years. The incidence of second hip fractures among women (2.5 cases per 100 person-years) was almost twice the incidence of second hip fractures among men (1.3 cases per 100 person-years). The median age at second fracture was 86 years and ranged from 53 to 98 years. In participants with 2 hip fractures, the median time between fractures was 4.2 years and ranged from 1 month to 33.3 years.

Following a first hip fracture, 2.5% of subjects (3.1% of women) experienced a second hip fracture within 1 year, 5.7% within 3 years, and 8.2% (9.7% of women) within 5 years (**Table 2**). In contrast, 15.9% of subjects died within 1 year of an initial fracture, and 45.4% of subjects died within 5 years of an initial fracture. Following an initial hip fracture, men had greater mortality compared with women, particularly during the first year of follow-up (24.4% in men vs 13.8% in women, $P = .03$). The 1-year and 5-year mortality following a second hip fracture was 24.1% and 66.5%, respectively.

As expected, individuals who sustained a second hip fracture were younger at the time of their initial hip fracture (Table 1). Fifty-eight percent of participants with a second hip fracture were independent in walking one-

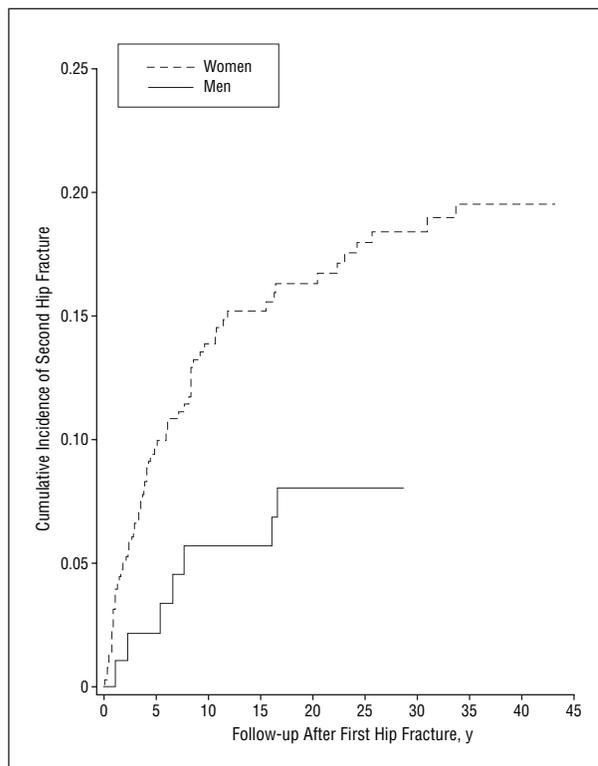


Figure. Cumulative incidence of second hip fracture among men and women with a first hip fracture (95 men and 386 women) from the Framingham Osteoporosis Study.

half to 1 mile, climbing a flight of stairs, and performing heavy housework at baseline, compared with only 27.1% of participants with 1 hip fracture. Individuals with a second hip fracture also had lower baseline incidence of stroke, falls, weight loss, and dementia compared with individuals with a first hip fracture only.

Older age was associated with an increased risk of second hip fracture after adjusting for sex. Low BMI and high functional status were also associated with an increased risk of second hip fracture in the age- and sex-adjusted analysis (**Table 3**). In multivariate analysis, older age and functional status remained statistically significant predictors of a second hip fracture. For every 5 years of advancing age at the time of a first hip fracture, the hazard ratio (HR) of developing a second hip fracture was 1.5 (95% confidence interval [CI], 1.1-1.8). High-functioning persons had more than twice the risk for a second hip fracture compared with moderate-functioning persons (HR, 2.7; 95% CI, 1.1-6.9). Although the HR was also elevated among those with baseline low functional status, it was not statistically significant (HR, 3.7; 95% CI, 0.9-14.8). Sex, falls, stroke, BMI, dementia, 4-year weight change, and nursing home residence were unassociated with the risk of second hip fracture in the age- and sex-adjusted or multivariate models. After repeating the analysis following imputation to produce complete data sets, the associations were unchanged.

COMMENT

We observed that a substantial number of persons who fractured their hip experienced a second hip fracture on

Table 2. Cumulative Incidence of Second Hip Fracture and Death in Men and Women With an Initial Hip Fracture

Follow-up, y	Cumulative Incidence of Second Hip Fracture ^a			Cumulative Incidence of Death ^b		
	Men (n = 95)	Women (n = 386)	Total (N = 481)	Men (n = 95)	Women (n = 386)	Total (N = 481)
0.5	0.0	1.3	1.0	21.1	9.6	11.9
1	0.0	3.1	2.5	24.4	13.8	15.9
2	1.1	5.0	4.2	33.0	22.8	24.8
3	2.2	6.6	5.7	43.9	31.1	33.6
5	2.2	9.7	8.2	56.3	42.8	45.4
10	5.7	13.8	12.2	80.2	70.5	72.4

^aBased on a cumulative incidence estimate accounting for variable length of follow-up and the competing risk of death.²²

^bBased on Kaplan-Meier estimates.

Table 3. Association Between Baseline Characteristics and the Risk of Second Hip Fracture

Predictor	Hazard Ratio of Second Hip Fracture (95% Confidence Interval)	
	Age and Sex Adjusted	Multivariate Adjusted ^a
Age, per 5 y	1.3 (1.1-1.5)	1.5 (1.1-1.8)
Female sex	1.5 (0.7-3.2)	1.0 (0.3-3.0)
Body mass index, per unit	0.9 (0.8-1.0)	1.0 (0.9-1.1)
4-y Weight change, per 10 lb	1.2 (0.9-1.5)	...
Stroke	0.9 (0.3-2.4)	...
Dementia	2.1 (0.8-5.3)	...
Nursing home residence	1.1 (0.3-4.9)	...
Prior falls	1.2 (0.5-2.4)	...
Functional status		
High vs moderate	2.6 (1.1-6.3)	2.7 (1.1-6.9)
Low vs moderate	2.5 (0.8-7.7)	3.7 (0.9-14.8)

SI conversion factor: To convert pounds to kilograms, multiply by 0.45.

^aAdjusted for age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), and functional status (n = 178). Ellipses indicate variable not included in the final model because bivariate $P > .10$.

the opposite side within 5 years. Many of these second hip fractures occurred more than 1 year following an initial hip fracture. Older age and high functional status at the time of an initial hip fracture were predictive of a second hip fracture.

The incidence rate of second hip fractures in the present study is consistent with previous reports.^{9-12,14} However, our study identified a greater overall incidence of second hip fractures and a longer median time between fractures compared with other studies. Findings from prior studies^{8,9,11,12,14,15} suggest that many second hip fractures occur within 1 year of initial fracture, while our study found that only 2.5% of persons with a first hip fracture went on to develop a second hip fracture within 1 year. These differences likely reflect the longer follow-up period in our study.

Our results indicate that, during the first year following a hip fracture, the risk of death was greater than the risk of subsequent hip fracture. Mortality following a hip fracture is greatest immediately after the event, and it begins to approach prefracture mortality rates by 6 months after a fracture.²⁴ Our study revealed that mortality was

particularly high among men, with 21.1% of men dying within 6 months of an initial hip fracture. Other investigations have confirmed this marked sex difference in mortality, much of which is attributable to an increased risk of death from infections in men during the first year after a hip fracture.²⁵ A better understanding of postoperative predictors of mortality is needed to differentiate individuals at risk of dying quickly following a hip fracture from individuals who are likely to live long enough to experience secondary fractures.

To the best of our knowledge, this is the first study to report mortality rates following a second hip fracture. We found that 1-year mortality following a second hip fracture (24.1%) was higher than 1-year mortality following a first hip fracture (15.9%). This may partially be explained by the older age of subjects at the time of a second hip fracture. However, comparing mortality rates following a first or second hip fracture in a subset of women of the same age with similar baseline characteristics, the mortality rates remained higher following a second hip fracture. This may suggest physiologic differences in recovery following a first or second hip fracture.

Our results indicated that age and functional status were the most important predictors of a second hip fracture. Studies^{12,14,16} found older age to be associated with an increased risk of first and second hip fractures; however, less is known about functional status and hip fracture. Most investigations have demonstrated a decreased risk of hip fracture among high-functioning persons,²⁶ yet our study found an increased association between high functional status and a second hip fracture. High functional status predicts improved physical recovery following an initial hip fracture,²⁷ which may result in increased opportunities for these individuals to survive and fall after the initial hip fracture.

Results of our study also suggest an increased risk of second hip fracture among low-functioning persons, although this finding was not statistically significant ($P = .07$). This apparent U-shaped relation between functional status and the risk of second hip fracture has been suggested in other investigations of first hip fracture.²⁸ We had limited power to fully describe this association because functional status was not measured until late in the study.

We hypothesized that 4-year weight loss would be a predictor of a second hip fracture, yet no such relation-

ship was observed. Instead, we found that persons experiencing weight loss before an initial hip fracture had increased mortality compared with persons without weight loss (results not shown).

Our study did not find an association between stroke, falls, dementia, or nursing home residence and the risk of second hip fracture. Other studies^{8,11,15} found dementia and stroke to be associated with an increased risk of second hip fracture. Given the methods used to diagnose neurological disease in these studies, misclassification is likely and may have affected the results. Findings from prior studies^{8,13} suggest an increased risk of second hip fracture among nursing home residents and those who fall. Our study had limited power to examine falls and residence as risk factors because information on these predictors was not collected until late in the study. It is also possible that some predictors may have changed following an initial hip fracture. The present analysis does not consider the effect of impediments after an initial hip fracture and may underestimate the true effect of certain risk factors.

The long follow-up period in this study may have introduced confounding because of improvements in surgical outcomes. The introduction of prophylactic antibiotics, efforts for early mobilization, better identification of persons at risk for cardiac complications, and improved selection of patients with femoral neck fractures to receive arthroplasty in place of internal fixation devices has led to substantial improvements in perioperative outcomes.^{29,30} Consequently, estimates of perioperative and 1-year mortality rates following a hip fracture have improved dramatically since the 1950s, and they approached current mortality rates by the early 1970s.³¹ To exclude secular differences in outcomes following hip fracture repair, we ran a stratified analysis excluding all hip fractures that occurred before 1974 (n = 70). The time to second hip fracture and risk factors for a second hip fracture remain unchanged in these analyses.

Several limitations of our study should be noted. First, certain predictors are missing a large amount of data. Missing data are primarily absent by study design because not all information pertaining to the risk of hip fracture was collected at early examinations. However, a study of hip fractures inevitably involves participants with frailty, and some individuals were not always available at examinations. We took several approaches to handling these missing data. Initially, we used only subjects with complete data ascertainment, resulting in estimates that are conservative. The associations were unchanged in our sensitivity analysis using multiple imputation. Finally, we performed a sensitivity analysis in which we excluded predictors with large amounts of missing data (functional status and weight change). The association between age, sex, BMI, and the risk of second hip fracture remained unchanged in this analysis. Second, although 71 second hip fractures is a large number compared with many studies of second hip fractures, this number is modest. Because the outcome was rare, particularly in men, we had limited power to detect statistically significant risk factors for a second hip fracture. Third, no information on bisphosphonate use was available. Because older persons are less likely to receive treatment with a bisphos-

phonate,⁴ it is possible that the use of these medications explains the association found between older age and an increased risk of second hip fracture. Given that bisphosphonates were not available until the mid 1990s, it is unlikely that the use of these medications alone explains our findings. Fourth, the study did not have information on other potential predictors of interest, including bone mineral density and visual acuity. Fifth, the population enrolled in the Framingham cohort did not include minority groups, and the results may not be generalizable to other populations. Despite these limitations, this study is important because we believe it is the first population-based study to describe the characteristics of men and women with a second hip fracture.

Few data exist on the secondary prevention of hip fractures. Given that some of the clinical trials that found a benefit in reducing hip fractures with pharmacological agents included a large number of women with prior non-vertebral fractures, there is reason to believe that treatment might be efficacious.³² However, a randomized trial of postmenopausal women selected based on risk factors for fracture (including history of hip fracture) found no reduction in hip fractures among the women taking risenedronate.³³ The lack of proven efficacy for the secondary prevention of hip fractures highlights the need for more studies in this specific population.

Given the findings of this study, a substantial number of persons who experience a hip fracture are at risk for a second hip fracture. There is adequate time between the first and second hip fractures for clinicians to intervene in an effort to reduce the risk of second hip fracture. Treatment with vitamin D is recommended for all persons with a hip fracture in an effort to improve bone mineral density and to reduce the risk of subsequent falls.^{34,35} Clinicians should give special attention to age and functional status at the time of the first hip fracture when determining whether additional therapies are appropriate in an effort to reduce secondary hip fractures.

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Author Contributions: Dr Berry had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Berry, Cupples, and Kiel. *Acquisition of data:* Hannan, McLean, Cupples, Beiser, Kelly-Hayes, and Kiel. *Analysis and interpretation of data:* Berry, Samelson, Hannan, Lu, Cupples, Shaffer, and Kiel. *Drafting of the manuscript:* Berry. *Critical revision of the manuscript for important intellectual content:* Samelson, Hannan, McLean, Lu, Cupples, Shaffer, Kelly-Hayes, and Kiel. *Statistical analysis:* Lu, Cupples, Shaffer, and Beiser. *Obtained funding:* Berry and Kiel. *Study supervision:* Kiel.

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Additional Contribution: Harris S. Yett, MD, provided information on secular trends in hip fracture repair.

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