Second Hip Fracture in Older Men and Women

The Framingham Study

Sarah D. Berry, MD, MPH; Elizabeth J. Samelson, PhD; Marian T. Hannan, DSc; Robert R. McLean, DS; Mei Lu, MS; L. Adrienne Cupples, PhD; Michele L. Shaffer, PhD; Alexa L. Beiser, PhD; Margaret Kelly-Hayes, EdD, RN; Douglas P. Kiel, MD, MPH

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 initial 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.

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.

### METHODS

#### 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. 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 1992 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. Dementia of all subtypes was assessed by neuropsychological testing and neurological examination using methods previously described. 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 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.

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Yes (n = 71)</th>
<th>No (n = 410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>77.2 ± 10.2</td>
<td>80.3 ± 9.5</td>
</tr>
<tr>
<td>Female sex</td>
<td>481</td>
<td>90.1</td>
</tr>
<tr>
<td>Weight, lb</td>
<td>128.4 ± 24.1</td>
<td>136.4 ± 27.0</td>
</tr>
<tr>
<td>Height, in</td>
<td>62.1 ± 2.9</td>
<td>62.3 ± 3.7</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.4 ± 3.7</td>
<td>24.5 ± 4.3</td>
</tr>
<tr>
<td>Estrogen use</td>
<td>386</td>
<td>1.6</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>480</td>
<td>0.9</td>
</tr>
<tr>
<td>Never</td>
<td>48.6</td>
<td>43.7</td>
</tr>
<tr>
<td>Former</td>
<td>32.9</td>
<td>38.3</td>
</tr>
<tr>
<td>Current</td>
<td>18.6</td>
<td>18.1</td>
</tr>
<tr>
<td>4-y Weight change, lb</td>
<td>-1.7 ± 9.7</td>
<td>-6.0 ± 12.7</td>
</tr>
<tr>
<td>Stroke</td>
<td>467</td>
<td>5.8</td>
</tr>
<tr>
<td>Dementia</td>
<td>344</td>
<td>11.5</td>
</tr>
<tr>
<td>Nursing home residence</td>
<td>254</td>
<td>4.8</td>
</tr>
<tr>
<td>Prior falls</td>
<td>207</td>
<td>33.3</td>
</tr>
<tr>
<td>No. of modified Katz Activities of Daily Living Scale items performed independently</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>4.8</td>
<td>8.1</td>
</tr>
<tr>
<td>2</td>
<td>7.1</td>
<td>5.4</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>4</td>
<td>85.7</td>
<td>84.2</td>
</tr>
<tr>
<td>No. of Rosow-Breslau Scale items performed independently</td>
<td>235</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>25.0</td>
<td>48.7</td>
</tr>
<tr>
<td>2</td>
<td>16.7</td>
<td>24.1</td>
</tr>
<tr>
<td>3</td>
<td>58.3</td>
<td>27.1</td>
</tr>
<tr>
<td>Functional status</td>
<td>High</td>
<td>61.8</td>
</tr>
<tr>
<td>Low</td>
<td>14.7</td>
<td>16.1</td>
</tr>
</tbody>
</table>

SI conversion factor: To convert pounds to kilograms, multiply by 0.45. Data are given as mean ± SD or as percentages. Calculated as weight in kilograms divided by height in meters squared. Because 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. Information on these predictors was not available throughout the study because 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. 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. Dementia of all subtypes was assessed by neuropsychological testing and neurological examination using methods previously described. Residence and history of falls within the past year were obtained from standardized questionnaires.

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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). 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. 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-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 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 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).

We observed that a substantial number of persons who fractured their hip experienced a second hip fracture on
Cumulative Incidence of Second Hip Fracture and Death in Men and Women With an Initial Hip Fracture

<table>
<thead>
<tr>
<th>Follow-up, y</th>
<th>Cumulative Incidence of Second Hip Fracture</th>
<th>Cumulative Incidence of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n = 95)</td>
<td>Women (n = 386)</td>
</tr>
<tr>
<td>0.5</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>1</td>
<td>0.0</td>
<td>3.1</td>
</tr>
<tr>
<td>2</td>
<td>1.1</td>
<td>5.0</td>
</tr>
<tr>
<td>3</td>
<td>2.2</td>
<td>6.6</td>
</tr>
<tr>
<td>5</td>
<td>2.2</td>
<td>9.7</td>
</tr>
<tr>
<td>10</td>
<td>5.7</td>
<td>13.8</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio of Second Hip Fracture (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age and Sex Adjusted</td>
</tr>
<tr>
<td>Age, per 5 y</td>
<td>1.3 (1.1-1.5)</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.5 (0.7-3.2)</td>
</tr>
<tr>
<td>Body mass index, per unit</td>
<td>0.9 (0.8-1.0)</td>
</tr>
<tr>
<td>4-y Weight change, per 10 lb</td>
<td>1.2 (0.9-1.5)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.9 (0.3-2.4)</td>
</tr>
<tr>
<td>Dementia</td>
<td>2.1 (0.8-5.3)</td>
</tr>
<tr>
<td>Nursing home residence</td>
<td>1.1 (0.3-4.9)</td>
</tr>
<tr>
<td>Prior falls</td>
<td>1.2 (0.5-2.4)</td>
</tr>
<tr>
<td>Functional status</td>
<td></td>
</tr>
<tr>
<td>High vs moderate</td>
<td>2.6 (1.1-6.3)</td>
</tr>
<tr>
<td>Low vs moderate</td>
<td>2.5 (0.8-7.7)</td>
</tr>
</tbody>
</table>

^a Adjusted 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.

Results of our study indicate that age and functional status were the most important predictors of a second hip fracture. Studies have found 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, 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, which may result in increased opportunities for these individuals to survive and fall after the initial hip fracture.

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. A better understanding of postoperative predictors of mortality is needed to differentiate individuals at risk of dying quickly following a hip fracture from those 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.

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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=0.07). 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. 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\textsuperscript{6,11,13} 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\textsuperscript{6,12} 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.\textsuperscript{25,30} 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.\textsuperscript{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 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. Financial Disclosure: None reported.

Funding/Support: This study was funded by grant N01-HC-25195 to the Framingham Heart Study from the National Heart, Lung, and Blood Institute; by grant 5R01-NS17950 from the National Institute of Neurological Disorders and Stroke; by grant 5R01-AG16495 from the National Institute of Aging; by grant R01 AR/AG 41398

Accepted for Publication: June 6, 2007.

Correspondence: Sarah D. Berry, MD, MPH, Institute for Aging Research, Hebrew SeniorLife, 1200 Centre St, Boston, MA 02131 (sarahberry@hsrca.harvard.edu).

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. Financial Disclosure: None reported.

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from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute of Aging; by a Harvard/Hartford institutional grant; and by grant P60 AG08812 from the Older Americans Independence Center.

Previous Presentations: This study was presented in part as an abstract at the 2006 Annual Scientific Meeting of the American Geriatrics Society; May 4, 2006; Chicago, Illinois; and at the 28th Annual Meeting of the American Society for Bone and Mineral Research; September 15, 2006; Philadelphia, Pennsylvania.

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

REFERENCES


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