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Height Loss Predicts Subsequent Hip Fracture in Men and Women of the Framingham Study

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Abstract

Background—Although height is a risk factor for osteoporotic fracture, current risk assessments do not consider height loss. Height loss may be a simple measurement that clinicians could use to predict fracture or need for further testing.

Objective—To examine height loss and subsequent hip fracture, evaluating both long-term adult height loss and recent height loss.

Methods—Prospective cohort of 3,081 adults from the Framingham Heart Study. Height was measured biennially since 1948, and cohort followed for hip fracture through 2005. Adult height loss from middle-age years across 24 years and recent height loss in elderly years were considered. Cox proportional hazard regression was used to estimate association between height loss and risk of hip fracture.

Results—Of 1,297 men and 1,784 women, mean baseline age was 66y (SD7.8). Average height loss for men was 1.06 inches (0.76), and for women was 1.12 inches (0.84). 11% of men and 15% of women lost ≥ 2 inches of height. Mean follow-up was 17y during which 71 men and 278 women had incident hip fractures. For each 1-inch of height loss, HR=1.4 in men (95%CI: 1.00, 1.99), and 1.04 in women (95%CI: 0.88, 1.23). Men and women who lost ≥ 2 inches of height had increased fracture risk (compared to 0 to <2 inches) of borderline significance: men HR=1.8, 95%CI: 0.86, 3.61; women HR=1.3, 95%CI: 0.90, 1.76. Recent height loss in elders significantly increased the risk of hip fracture, 54% in men and 21% in women (95%CI: 1.14, 2.09; 1.03, 1.42, respectively).

Conclusions—Adult height loss predicted hip fracture risk in men in our study. Recent height loss in elderly men and women predicted risk of hip fracture.

Keywords

Hip fracture; population study; height loss; osteoporosis; aging; cohort study

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Introduction

While the total health care costs in the United States of osteoporotic hip fractures alone is estimated at \$18 billion dollars, hip fractures cause more deaths, disability and increased costs than all other fractures combined.¹⁻⁶ Over 300,000 hip fractures occur each year in the U.S., often leading to significant functional decline, mortality and institutionalization.¹⁻⁴ The number of hip fractures grows as the population of elders increases. The average woman over age 50 in the United States has a 50 percent risk of osteoporotic fracture in her remaining lifetime, while one in four men over age 50 will have such a fracture in his lifetime.^{2,4,7} In the first year after hip fracture, the all-cause mortality rate is 15-24 percent higher in those with hip fracture compared to individuals of similar age and sex without a hip fracture. Incidence of hip fracture rises dramatically with age, especially in elderly women,⁷ although elderly men also have an increased incidence of hip fracture with increasing age.

Although height is a risk factor for osteoporotic fracture, the current risk assessment tools only consider a patient's current height¹²⁻¹⁴ and not the amount of height loss, which may be a better measure of future fracture risk. Also there are health disparities in access to DXA and other imaging technologies used to estimate clinical osteoporosis status in patients. Height loss is a simple, easily measured attribute that clinicians may be able to use to predict fracture. It has been generally assumed that height loss is related to osteoporotic fractures because it is a marker for vertebral fracture (itself a predictor of hip fracture).¹¹ It is unclear if heights measured over time are predictive of hip fracture. Although a number of studies have examined risk factors for hip fracture,^{5-7,13,15,16} we were interested in those factors that may indicate change for an individual and may provide an early indication to seek diagnosis or to begin treatment or intervention. Height loss is easily measured and may indicate potential for subsequent hip fracture and thus could serve as an alert to clinicians and elders to seek medical evaluation.

Several studies have reported an association between height and hip fracture,¹⁷⁻²⁰ concluding that taller persons had a higher risk of fracture, but the studies did not consider height loss. The few studies that examined height loss descriptively were limited by including only those subjects who sought medical attention,²¹⁻²³ or by including large proportions of subjects ages 20-45, a time when little or no height loss occurs.^{21,24,25} Further, these height loss studies were typically cross-sectional and height loss was based on a subject's recall of her/his height.²⁶ Thus, although loss of height may be used clinically and anecdotally in the evaluation of elderly patients,²⁷⁻²⁹ few studies have adequately evaluated height loss and hip fracture.

The purpose of this paper was to examine adult height loss over time, as an early indicator of risk for incident hip fracture. Using data from the Framingham Study, we evaluated the relation of height loss and hip fracture in men and women of the Framingham cohort in two ways. First, long term adult height loss was evaluated for risk of subsequent hip fracture. Secondly, recent height loss in elderly individuals was investigated for a possible association with hip fracture since many clinical practices may only have recent height measures for their patients.

Methods

Framingham Study Participants

The Framingham cohort has been followed biennially for over 50 years, starting in 1948 with 5,209 participants, ages 28-62. The population-based cohort was initiated to study risk factors for cardiovascular disease and was composed of a two-thirds sample of the town of

Framingham, Massachusetts, USA. Recruitment details and general examination procedures of the Framingham Study have been described elsewhere.²⁷ In general, at each biennial visit participants receive an extensive physical examination, comprehensive questionnaires, anthropometric measurements, and assessment of cardiovascular and other risk factors, gathered by trained clinical personnel. The cohort is carefully followed for medical events including hip fractures with less than one percent loss to follow-up.^{28,29} For the current study, Framingham Study participants who survived to the 1974-75 biennial examination were included if they had height measured within one exam. This time frame for the current study was chosen as the baseline in order to have both a sufficient number of preceding height measurements for the assessment of long-term adult height loss, and a substantial follow-up time for incident hip fracture occurrences following baseline. Potential confounders were obtained from the baseline examination and included sex, age (years), and height (inches). Since hip fracture was examined following these height measurements, individuals with hip fractures occurring at baseline or previously were excluded from the analysis. Of the 5,209 participants in the Framingham Study, 3,081 survived to the 1974-75 baseline examination, had height measured, and had not previously fractured a hip. All study protocols and procedures have been approved by the Institutional Review Board of Hebrew SeniorLife and Boston Medical Center.

Height Measures

Starting in 1948, height has been assessed in the Framingham cohort, measured in inches using standard techniques and recorded to the nearest quarter inch (0.6 cm). As height was measured in inches rather than centimeters, we report the methods and results using inches. Standing height was measured for participants in their stocking feet, using an anthropometer with the shoulder blades and back of the head touching the anthropometer and eyes directed straight ahead at eye level. All Framingham clinic procedures undergo a test-retest reliability study about every 4-6 years and the height measurements have excellent measurement reliability (ICC>0.99).

Long-Term Adult Height Loss—Long-term adult height loss was calculated as the difference between height measured at the initial Framingham examination (1948) and the baseline examination for this study (1974-75), representing adult height loss over 24 years as seen in Figure 1. For those participants missing baseline height (7 percent), their height loss was calculated from the initial 1948 examination to the examination immediately preceding baseline (two years prior). Study participants were followed for their time-to-fracture from the baseline examination (1974-75) through 2005. The long-term height loss time period was set to a calendar time and was not a function of how long participants were followed. If Framingham Study participants were alive in 1974, then they had long-term height loss calculated and were then followed for events. The study participants all had long-term height loss data over the 'exposure' time frame (when most were middle-aged), before follow-up for hip fracture or event as seen in Figure 1.

Recent Elderly Height Loss—More recent height loss at elderly ages was examined by estimating the risk of hip fracture within 2 years of height loss as seen in Figure 2. Recent height loss was calculated as the two-year loss from the preceding exam for each biennial exam at risk after baseline examination in 1974-75 to 2005). Hip fracture over each subsequent two-year interval was then used as the outcome. The recent height loss occurred within the two-to-four year time frame before the possible hip fracture occurrence period (i.e., every two-year period was evaluated for risk of hip fracture).

We did not evaluate long-term height loss over the entire study interval. We were interested in examining a time frame when most individuals were middle-aged (the height loss that

occurred during the long-term time frame, 1948-1972) and when participants were elderly (the height loss that occurred two years before the interval examined for hip fracture in this portion of the study).

Hip Fracture

The Framingham Original Cohort has been followed prospectively for hip fracture. Osteoporotic hip fractures were defined as incident fractures of the proximal femur occurring either after age 50 or in postmenopausal women. Hip fractures were continuously ascertained in the cohort through review of hospitalizations and death records, and direct query of subjects, as detailed by Kiel et al.²⁸ Incident hip fractures are confirmed by medical, hospital and surgical records, including radiographic and operative reports. Over 97% of the hip fracture cases were due to falling. For this study, hip fracture was defined as a first-time fracture of the proximal femur that occurred in the absence of overwhelming trauma (e.g., motor vehicle accident).

Statistical Methods

Cohort members were followed from baseline examination (when ages ranged from 38-64 years), accumulating person-years at risk until the first occurrence of hip fracture, death, last contact with the participant, or the end of follow-up (December 31, 2005, for all study participants). Cox proportional hazards regression was used to calculate hazard ratios and 95% confidence intervals for height loss and risk of hip fracture. In the models, we controlled for baseline age and maximum adult height (height at initial 1948 examination) since age is an important determinant of hip fracture and height loss, and taller persons are at a higher risk of hip fracture. In addition to the continuous measure of height loss in inches, we also examined ≥ 2 inches of height loss versus <2 inches loss. We modeled this ≥ 2 inches of height loss as an indicator variable and used Cox proportional hazards regression models to estimate the relative increase in the risk of hip fracture for this degree of height loss compared with the group with no or little height loss. The arbitrary cut-point of 2-inches of height loss was chosen a priori as clinically meaningful, perhaps meaningful to individuals and to allow comparison to other literature. We couldn't examine the extremes of height loss (e.g., > 3 -inches) as too few participants had this amount of height loss.

To calculate risk for recent height loss, a competing risk model for survival analysis, allowing for time-varying effects of recent height loss, was used.^{30,31} Recent 2-year height loss was analyzed as a time-varying covariate within proportional hazards models with the risk set based on evaluating the risk over time as each hip fracture event occurred. This analysis evaluated the risk of incident hip fracture within a two-year time frame, as a function of recent height loss (loss in the previous two years). We also examined these models evaluating recent height loss and competing risk of death, using a standard approach as described by Therneau and others.³⁰⁻³¹

All analyses were conducted separately for men and women. The proportional hazards assumption was satisfied for Cox regression analyses of all models among the men and the women. Relative hazards and 95% confidence intervals were derived from these analyses. For all statistical analyses, SAS/STAT software version 9.1 (SAS Institute, Cary, North Carolina) was used.

Results

Table 1 lists the baseline characteristics of the participants included in the analysis. Of the 1,297 men and 1,784 women in our study, mean baseline age was 65 years (7.6, SD) and 66 (7.9), respectively. Average height loss over this time period for men was 1.06 ± 0.76 inches

while for women the average loss was 1.12 ± 0.84 inches. Eleven percent of the men and 15 percent of women lost ≥ 2 inches of adult height over the 24 years from the initial 1948 examination. Median duration of follow-up from the end of the 24-year height loss period was 17 years (range 6-31 years) during which 71 men and 278 women had incident hip fracture. Of the Framingham Cohort participants who were not included in this analysis, 95% died prior to the baseline exam (1974-75), and compared with those included, they were older and heavier at the initial 1948 examination; however, their mean height only differed by 0.3-inches on average. Characteristics of baseline height measures and height loss variables are presented in Table 2. Mean long-term height loss was slightly more than an inch for both men and women. Within the follow-up from baseline examination to December 2007, there were 2781 persons with recent height loss information (for men the mean was -0.14 inches per two-year period ($\pm$ SD of 0.70), for women the mean was -0.19 ($\pm$ SD of 0.81)).

For each 1-inch of long-term adult height loss, when considered as a continuous variable, the HR for hip fracture was 1.4 in men (95%CI: 1.00, 1.99, and the HR was 1.04 in women (95%CI: 0.88, 1.23). Although of borderline statistical significance, both men and women who lost 2 or more inches of height were at increased fracture risk, even after adjustment for baseline age and height (Table 3), compared to the referent group (0 to <2 inches): for men, HR=1.8, 95%CI: 0.86, 3.61, while for women, HR=1.3, 95%CI: 0.90, 1.76. Thus, long-term height loss was not significantly associated with hip fracture in women (HR=1.04), or only moderately for women who lost 2 inches or more of height with confidence intervals that included the null value. In men, however, long-term height loss predicted subsequent hip fracture, with a borderline statistical result for 2 inches or more of height loss and when considered as a continuous measure, a 40% increased risk of hip fracture per inch of height lost. Age, a well established risk factor for fracture, also showed a 30% increased hip fracture risk for each 5 years of aging in this study (data not shown). These results were similar with additional adjustment for maximum height.

Table 3 also reports the Cox regression analysis for recent height loss, defined as the 2-year loss between adjacent biennial exams, and subsequent hip fracture. Recent height loss significantly increased an individual's risk of hip fracture, by 54% for men and 21% for women. Additional analyses that examined competing risks of death were undertaken to examine possible survivor bias. The results for recent height loss predicting hip fracture were unchanged by considering competing causes of mortality.

Discussion

This large, population-based study indicated a relation between long-term adult height loss (per inch) and subsequent hip fracture in men but not women. We also found that men with long-term height loss of 2-inches or more had nearly twice the risk of fracture than men with less height loss, albeit of borderline statistical significance. However, both elderly men and women with recent height loss were at increased risk for incident hip fracture. The major reason for the apparent different results for long-term and recent height loss in our study is that they address two different time frames. Long-term height loss occurred between 1948-1971 when many study participants were middle-aged and not yet elderly. Recent height loss occurred within the two-to-four year time frame before the possible hip fracture occurrence period for this height loss variable, when many study participants were elderly. In this study, recent height loss was associated with a 21%-54% increased risk for hip fracture within the subsequent two year period per inch of height lost. Recent height loss had an effect on hip fracture risk similar to that of five years of age. Thus, recent height loss during elderly ages seems to be an easily measured attribute that indicates a 2-year risk for subsequent hip fracture. Given that most hip fractures occur in elderly persons, a key finding

is that this recent height loss, even after adjusting for age, indicates increased risk for hip fracture. To our knowledge, this study is the first prospective, population-based study of both men and women to evaluate the association between measured height loss in elderly individuals and hip fracture.

In 1948, Fuller Albright first described a clinical syndrome that he called 'senile osteoporosis' in which elderly patients complained of back pain, lost height, and had an increased tendency to fracture vertebrae and long bones.^{32,33} Since that time, loss in height with increasing age has been documented among adults.^{18,21,22,33-38} Reduced height occurs for both sexes, but the loss is greater in women. Loss of height is most likely caused mainly by spinal changes, (e.g., vertebral fractures, weakening of muscle groups, postural changes, disc degeneration, spinal deformities, kyphosis). Like osteoporosis, height loss starts around age 45 and continues with age.^{15,21,22,38} Since the 1970s, several researchers have noted that trabecular sites, such as vertebral bone, lose bone preferentially to cortical sites, such as the femur.^{34,39-41} Numerous studies have also noted that the earliest osteoporotic fractures occur in the spine and most distal portions of the wrist, sites composed primarily of trabecular bone, while osteoporotic fractures of the femur (ranging from 50% - 90% cortical bone) often occur later, after ages 70-80. Noting the earlier trabecular bone loss, Thickman hypothesized that trabecular bone may be more sensitive for the early detection of osteoporosis.⁴² Thus, events linked to height loss (whether bone-related or not) appear to underscore the possible value of evaluating whether height loss could indicate risk of subsequent hip fracture in older adults.

To our knowledge, only one published population study has shown that height loss over time was predictive of hip fracture⁴³ among the mostly middle-aged participants. Moayyeri et al. used the EPIC Norfolk cohort of middle-aged adults who reported 122 hip fractures over a mean follow-up of 7 years, and found participants with a height loss > 1 cm/year compared with those with no height loss were at 3-fold increased risk of future fracture. They reported that the magnitude of fracture risk related to this height loss was comparable to past history of fracture and an additional 14 years of age. Several anecdotal studies have evaluated height loss and fracture even though loss of height is often used clinically in the evaluation of elderly patients.²⁴⁻²⁶

Although height is a major focus in the pediatric and physical anthropology literature, adult height loss has garnered relatively less attention in the medical literature. Several early anthropology studies describe cross-sectional assessment of height and age-related decline noted a range of 1.3 cm to 4.0 cm of loss per decade;³⁵⁻³⁷ however, these studies included a large proportion of subjects aged 20-45, a time when little or no height loss occurs. Galloway²¹ analyzed height loss for adults over 50, based on recall of height at age 25 and current measurement, and reported that while most participants did not recognize that they lost height, over 90 percent had height loss. The few longitudinal anthropologic studies only considered a 10-year time span with height measured at two points,^{22,34,38} however, typically had few subjects over age 70. Cline et al²² noted a 1.8 to 2.3 cm average decline across 10 years in participants aged 75-85 years. The Normative Aging Study³⁸ of male veterans reported average height loss of 4-cm at 10-year follow-up. Our study considered a 24-year span from middle-age to older adult age for long-term height loss as well as a shorter term of two years at a time when participants were elderly, in our evaluation of height loss and hip fracture.

There are several potential limitations to our study. Non-differential error in the measurement of height over time is a possibility as multiple members of the Framingham clinic staff obtained the height measurements across time, although height was measured using the same protocol and has a high reliability. If variation in height measurement was

present in our study, this error is likely to result in some bias towards the null, inferring that the estimated results are conservative. Also height measurement differs depending on the time of day when it was measured (typically, those measured earlier in the day are slightly taller than if they were measured later in the day), thus there will be some non-differential misclassification of height. Time of day at height measurement was not recorded, but we believe the effect to be a minor fluctuation, i.e., within the 1/4 inch recorded or minimal, since no exams were ever performed within an individual's first waking hour. Thus, the effects of height loss found in these data are conservative estimates, and are unlikely the result of a systematic bias (e.g., differential recall or self-report) in the measurement of height.

Loss to follow-up is a concern in cohort studies. The Framingham Study has a long record of high participation and small loss to follow-up (six percent overall). The data have been systematically collected biennially since 1948 by trained clinical personnel. In addition, those members not attending a particular Framingham examination were still followed for demographic, morbidity and mortality information. Despite potential concern that Framingham Study participants may not reflect the general population, study subjects had similar age-specific mortality rates as the town of Framingham⁴⁴ where they comprised only 3-5% of the 2000 census population, and their hip fracture rates follow the same age trend that was seen in national data.²⁸ The Framingham Study is relatively large and population-based rather than composed of volunteers or those who already had disease. Also, despite our analyses showing no effect from competing causes of death in our cohort, the recent height loss results may have been affected by survivor bias within the 2-year time frame. If height loss does affect fracture risk, some elderly cohort subjects with loss in stature may not have survived long enough to experience a hip fracture, resulting in effect measures biased toward the null.

Height loss may be due to many factors including weakening of the muscle groups, postural changes, disc degeneration, frailty, joint space narrowing and spinal deformities. Height loss may also be due to kyphosis (paraspinal muscle weakness and bone loss) which may contribute to fracture risk. No information is available on muscle strength, arm span or posture. Hip fractures are not entirely due to bone density; while we cannot tease out an exact effect, we believe that height loss is a marker for these many factors. These issues may lead to height loss, or are factors further back in the possible causal pathway, leading to height loss as a possible marker.

There are also other limitations. Framingham Study participants are primarily Caucasian men and women, limiting the generalizability of our study to other racial or ethnic groups. Also, it is possible that height loss is a marker for unmeasured covariates such as poor nutrition or impaired muscle strength, and the observed associations simply reflect a deficiency in other variables not considered in our study.

This study also has a number of strengths. To the best of our knowledge this is the first study to examine the longitudinal association between hip fracture and measured height loss in a large, population-based, elderly cohort that includes both men and women. We were able to examine long-term adult height loss across 24 years and its effect upon hip fracture with a median follow-up of 16 years as well as the effect of recent height loss during elderly years. Finally, hip fractures were rigorously confirmed by medical records abstraction, reducing the potential for misclassification of the outcome.

Conclusions

This study suggests that clinically measured height loss is associated with subsequent hip fracture in men and women in our population-based study. Height loss was associated with 40-54% increased risk of hip fracture in men for both long-term and recent height loss, whereas older women with recent height loss had a 21% increased risk of hip fracture. The major objective of this paper was to investigate height loss as an easily available indicator for incident hip fracture. The number of people with osteoporosis and the enormous personal and economic costs of fracture, point to the need for earlier sentinel events, especially those that may be apparent to patients as well as clinicians that may prompt evaluations in those individuals apt to fracture. Recent height loss in both elderly men and women appears to provide a simple indication of those individuals at risk for hip fracture. Those elderly persons with recent height loss may benefit from follow-up with diagnostic procedures and interventions (both osteoporotic-based and falls prevention) prior to any future fracture. Long-term adult height loss predicted hip fracture in men and thus may provide an early indicator of those men at risk for hip fracture.

Bone densitometers can be used to measure bone mass but this technology is not available to all individuals or clinicians. Quantitative computed tomography can also be used to detect osteoporosis however, it is costly and exposes the patient to significant amounts of radiation. Height loss may provide a simple alternative that can be used to assess the need for further diagnostic procedures and interventions. Using height loss, particularly in elderly men and women, may enhance the ability of currently used risk assessment tools such as FRAX to predict absolute fracture risk. In the office setting, looking for long term and short term height loss by measuring height at each visit may allow clinicians additional insights into the possible need for diagnostic procedures or that may indicate their patients' tendency towards fracture. Finally, this study suggests that recent height loss may identify those older individuals at highest risk for hip fracture, a major focus in osteoporosis research with obvious tremendous benefit.

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Figure 1.
Long-term height loss and time to hip fracture analysis, the Framingham study

Figure 2.
Recent height loss and 2-year risk of hip fracture analysis, the Framingham Study

TABLE 1

Descriptive characteristics of study participants at baseline (1974-1975), Framingham Original Cohort.

Characteristics	Men N=1297	Women N=1784
Baseline mean Age (years)	65 (7.6)	66 (7.9)
Age range	53-84	53-85
Height (inches)	67.8 (2.7)	62.7 (2.4)
Weight (pounds)	170 (26.0)	142 (26.5)
Person-years of follow-up (median)	16	18
Number of incident hip fractures	71	278

Mean (standard deviation), except where noted

TABLE 2

Height loss measures, Framingham Original Cohort.

	Men	Women
Long-term height loss from initial 1948 examination (inches) over 24 years of follow up	1.06 (0.76)	1.12 (0.84)
Categories of long-term height loss		
0 to < 2 inches	89%	85%
Two or more inches	11%	15%
Recent elderly height loss *	-0.14 (0.70)	-0.19 (0.81)

* most recent and available 2-year height change preceding fracture, n=2781 of whom 327 had a hip fracture Mean (standard deviation), except where noted

Mean (standard deviation), except where noted

TABLE 3

Adjusted hazard ratios for hip fracture by height loss group among men and women in the Framingham Study (1974-2005)

Type of Height Loss	Age and Height Adjusted Hazard Ratio (95% CI)	
	MEN	WOMEN
Long-Term Height Loss		
0 to < 2 inches	1.00 (referent)	1.00 (referent)
2 or more inches	1.8 (0.86, 3.61)	1.3 (0.90, 1.76)
Per 1-inch of height loss	1.4 (1.00, 1.99)	1.04 (0.88, 1.23)
Recent Elderly Height Loss		
Per 1-inch of height loss	1.5 (1.14, 2.09)	1.21 (1.03, 1.42)

Proportional hazards model adjusting for age and height.