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Proximal Humerus Fractures and the Risk of Subsequent Hip Fracture: Timing is Everything

- In osteoporosis, the rate of bone regeneration fails to keep up with the rate of bone degeneration.
- Fragility fractures in individuals with osteoporosis are debilitating, expensive and lethal.
- Having a fracture associated with osteoporosis significantly increases the risk of subsequent hip fracture.
- 25% of patients who have a hip fracture will die within the first year following the hip fracture.
- 70% of proximal humerus fractures occur in women.
- Having a proximal humerus fracture increases the risk of having a hip fracture 6-fold within the first year following the humerus fracture.
- Interventions and medical treatments can substantially decrease the risk of subsequent hip fractures as soon as 3-6 months after initiation of treatment.

Osteoporosis and associated fragility fractures are a major health concern and a source of significant morbidity and mortality around the world. For the year 2006, it was estimated that in the United States the economic burden associated with hip fractures alone might be in excess of \$20 billion dollars. Given the enormous social and monetary costs of hip fractures, their prevention is a pressing concern. It is well established that patients having had a single fragility fracture are at significantly increased risk of having a second fracture in the future. A history of proximal humerus fractures (Figure 1) also appears to be a risk factor for other incident fractures, including those at the hip. These data suggest that a fracture of the proximal humerus may be predictive of increased risk for a subsequent hip fracture, however the methodology of previous studies did not control for many important variables. Interestingly, the mechanism

of proximal humerus fractures is similar to that of hip fractures in that patients are unable to break their forward or oblique fall and therefore land directly onto their shoulder or hip. Given the similar mechanism of fracture, it is intuitive that the timing of a hip fracture would be relatively close to the timing of a proximal humerus fracture in contrast to other osteoporotic fractures.

We hypothesized that patients who sustain a proximal humerus fracture will be at higher risk for a subsequent hip fracture and that the hip fractures would tend to occur within the five years after the fracture of the proximal humerus.

Methods

The Study of Osteoporotic Fractures is a prospective multicenter cohort study of 9,704 women age 65 years and older who were enrolled from September 1986 to October 1988 in four separate geographic areas

of the United States. Women were recruited if they were over the age of sixty-five, community dwelling, ambulatory, and had no history of bilateral hip replacements. The women were followed prospectively for up to 10 years at regular intervals. The participants attended seven examinations at approximately two-year intervals and were contacted by phone or postcard every four months to ascertain fracture history with over a 99% follow-up rate and 90% accuracy.

The original Study of Osteoporotic Fractures' cohort included 9,704 women, of whom 1,655 (17%) were excluded from our study due to missing data regarding prior fracture status or age, lack of complete follow-up, history of hip or humerus fracture prior to Exam 2, or missing bone mineral density data. A total of 8,049 (83%) women, therefore, were considered for our present study and their information was used in the univariate Cox regression



Figure 1: Low energy proximal humerus fracture a common "fragility fracture."

between incident humerus fracture and the risk of subsequent hip fracture. STATA (StataCorp LP, College Station, Texas) statistical software was used for all analysis. All models were adjusted for current age and total hip bone mineral density. Each observation in the Cox regression was left-censored at the age upon entering the study and either ended at the hip fracture or was right-censored at the end of the follow-up period.

In order to examine whether or not the risk of a subsequent hip fracture attributable to an incident humerus fracture changes over the time elapsed after the humerus fracture, two multivariate models were run categorizing time after humerus fracture as a time-varying variable. The three post-humerus fracture intervals were: a) <1 year, b) 1-5 years, and c) >5 years after the humerus fracture, with subjects not experiencing an incident humerus fracture utilized as the reference group for all analyses.

Results

Three hundred and twenty-one women sustained a proximal humerus fracture and forty-four sustained a subsequent hip fracture. The hazard ratio for hip fracture for subjects with a fracture of the proximal humerus relative to those without after multivariate analysis was 1.83 (95% C.I. 1.32 - 2.53). After multivariate adjustment, this risk appeared attenuated but was still significant (1.57; 95% C.I. 1.12-2.19). The risk of subsequent hip fracture after proximal humerus fracture was highest within 1 year of the proximal humerus fracture with a Hazard Ratio of 5.68 (95% C.I. 3.70 - 8.73). This association was not significant after the first year, with a Hazard Ratio of 0.87 (95% C.I. 0.48 - 1.59) for the time period between 1-5 years post humerus fracture and 0.58 (95% C.I. 0.22 - 1.56) at >5 years.

Discussion

In this cohort of older, community dwelling women, incident proximal humerus fractures significantly

analyses. A total of 1,128 (12%) were excluded from the final multivariate analysis due to missing data for one or more covariates, leaving 6,921 (71%) women to be analyzed.

Cox proportional hazards models were used to quantify the association

Risk factor	N	HR (95% C.I.)	p
Total hip bone mineral density (per 1 SD decrease*)	8049	2.11 (1.94 – 2.29)	<0.001
Humerus fracture	8049	1.83 (1.32 – 2.53)	<0.001
Non-humerus, non-hip fracture	8049	1.43 (1.20 – 1.72)	<0.001
Height at 25 years (per 10 cm)	7904	1.41 (1.24 – 1.61)	<0.001
Depth perception (per 10 times SD of 4 Howard-Dohlman optical distance scores (cm))	7851	1.43 (1.13 – 1.82)	0.003
Weight gain since age 25 (per 10 kgs)	7823	0.94 (0.85 – 1.04)	0.2
Maternal history of hip fracture after 50 yrs	6153	1.33 (1.06 – 1.66)	0.013
Estrogen use	8048	1.09 (0.86 – 1.40)	0.5
Use of long acting benzodiazepines at baseline	8008	0.98 (0.75 – 1.23)	0.9
Self related health status (1-5)	8049	1.33 (1.20 – 1.46)	<0.001
Walking for exercise	8049	0.85 (0.73 – 0.99)	0.04
On feet less than 4 hours a day	8046	1.27 (1.04 – 1.55)	0.02
Use of arms to stand	8046	1.37 (1.12 – 1.67)	0.002
History of falls	8049	1.38 (1.18 – 1.61)	<0.001

Table 1: Effect of risk factors for hip fracture, adjusted for age and total hip bone mineral density. * 1 SD = 0.133 g/cm² Total hip bone mineral density adjusted for age only.

Risk factor	HR (95% C.I.)	p-value
Total hip Bone mineral density (per 1 SD decrease)	2.08 (1.91 – 2.27)	<0.001
Self related health status (1-5)	1.24 (1.12 – 1.38)	<0.001
Height at 25 years (per 10 cm)	1.39 (1.22 – 1.59)	<0.001
History of falls	1.29 (1.10 – 1.52)	0.002
Depth perception	1.53 (1.19 – 1.97)	0.001
Non-humerus fracture	1.28 (1.06 – 1.55)	0.01
Humerus fracture	1.57 (1.12 – 2.19)	0.009

Table 2: Final multivariate Cox proportional hazards model for hip fracture, including humerus fracture as a risk factor. (N=6921 subjects).

increased risk of subsequent hip fracture. In particular, the risk of a subsequent hip fracture was six-times higher within the first year following the proximal humerus fracture, even when controlled for other important risk factors in a multivariate analysis. This association is not statistically significant at time intervals greater than one year after the incident humerus fracture. Although our study could have missed a modest persistent association between humerus fractures and incident hip fractures occurring after one-year of follow-up, the excess risk of hip fractures attributable to a prior humerus fracture clearly sharply waned after one-year of follow-up.

The results of the current study have significant implications in the clinical evaluation, treatment, and prevention of future fractures in patients sustaining a proximal humerus fracture. They demonstrate that the most concerning time frame for the risk of a subsequent hip fracture is

within a year of a proximal humerus fracture, and therefore intervention following a humerus fracture should be initiated without delay to reduce risk of subsequent fractures. Studies have suggested that oral bisphosphonates begin to reduce the risk of fractures within 3 to 6 months after being started. In addition to initiation of medical treatment for osteoporosis, steps should be taken in the prevention of falls in the at-risk population, as nearly 80% of proximal humerus fractures and 90% of hip fractures are related to falls from a standing height. A recent meta-analysis demonstrated the need for a multifaceted approach in the prevention of falls in hospitals and nursing homes and that no single intervention had a significant effect in a hospital setting. And although this study evaluated patients in a hospital or nursing home setting and not community ambulators as in our study, they too likely needed a multifaceted approach to the prevention of further

falls whether it be assistive devices at home, adjustment of medications, or the evaluation of environmental factors that lead to initial falls as well as the initiation of medical therapy for osteoporosis. A recent statement on the guidelines for the prevention of falls in the elderly was formulated by the American Geriatric Society, British Geriatric Society, and American Academy of Orthopaedic Surgeons and serves as a useful resource in the evaluation and prevention of falls in the geriatric population. It is also important to note that the risk of subsequent fracture is increased after proximal humerus fracture not only in women but also in men as noted by Ettinger et al.

In conclusion, the current study supports our hypothesis that proximal humerus fracture is an independent risk factor for subsequent hip fracture. Importantly, the time of greatest risk is the first year following proximal humerus fracture, and the risk of

Period	Hazard ratio, adjusted for age and Bone mineral density (95% C.I.)	Hazard ratio, adjusted for age, Bone mineral density and variables from the final multivariate model* (95% C.I.)
Before the humerus fracture	1.00	1.00
First year after the humerus fracture	6.16 (4.01 – 9.44)	5.68 (3.70 – 8.73)
1 - 5 years after the humerus fracture	1.16 (0.67 – 2.02)	0.87 (0.48 – 1.59)
> 5 years after the humerus fracture	0.64 (0.24 – 1.71)	0.58 (0.22 – 1.56)

Table 3: The risk of a hip fracture over time following a humerus fracture.

incident hip fracture attributable to prior humerus fractures wanes sharply after that. This small window of time provides an opportunity to implement medical and environmental interventions that may decrease the risk of subsequent hip fractures and their cost to the patient and to society.

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