Refractures in Patients at Least Forty-five Years Old

A Prospective Analysis of Twenty-two Thousand and Sixty Patients

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Background: Individuals who sustain a low-energy fracture are at increased risk of sustaining a subsequent low-energy fracture. The incidence of these refractures may be reduced by secondary preventative measures, although justifying such interventions and evaluating their impact is difficult without substantive evidence of the severity of the refracture risk. The aim of this study was to quantify the risk of sustaining another fracture following a low-energy fracture compared with the risk in an age and sex-matched reference population.

Methods: During the twelve-year period between January 1988 and December 1999, all inpatient and outpatient fracture-treatment events were prospectively audited in a trauma unit that is the sole source of fracture treatment for a well-defined local catchment population. During this time, 22,060 patients at least forty-five years of age who had sustained a total of 22,494 low-energy fractures of the hip, wrist, proximal part of the humerus, or ankle were identified. All refracture events were linked to the index fracture in the database during the twelve-year period. The incidence of refracture in the cohort of patients who had sustained a previous fracture was divided by the "background" incidence of index fractures within the same local population to obtain the relative risk of refracture. Person-years at-risk methodology was used to control for the effect of the expected increase in mortality with advancing age.

Results: Within the cohort, 2913 patients (13.2%) subsequently sustained a total of 3024 refractures during the twelve-year period. Patients with a previous low-energy fracture had a relative risk of 3.89 of sustaining a subsequent low-energy fracture. The relative risk was significantly increased for both sexes, but it was greater for men (relative risk = 5.55) than it was for women (relative risk = 2.94). The relative risk was 5.23 in the youngest age cohort (patients between forty-five and forty-nine years of age), and it decreased with increasing age to 1.20 in the oldest cohort (patients at least eighty-five years of age).

Conclusions: Individuals who sustain a low-energy fracture between the ages of forty-five and eighty-four years have an increased relative risk of sustaining another low-energy fracture. This increased risk was greater when the index fracture occurred earlier in life; the risk decreased with advancing age. Secondary preventative measures designed to reduce the risk of refracture following a low-energy fracture are likely to have a greater impact on younger individuals.

In the aging population, fragility fractures are responsible for substantial morbidity and mortality and place an economic drain on limited health-service resources[1]. Given that osteoporosis is clinically undetectable but very common, affecting a third of women over the age of sixty years[2], it is important to identify those individuals who are most at risk for fracture in order to direct appropriate interventions to these individuals.

Where health-service resources are limited, applying secondary prevention to high-risk groups may be more feasible economically than treating a less narrowly defined population. Several studies have indicated that patients with prior fractures, whether or not due to osteoporosis[3-5], may be at an increased risk of sustaining a future fragility fracture. These patients represent a group that could benefit from interventional strategies. The literature addressing the magnitude of this increased risk was summarized recently, with a statistical synthesis of the results[6]. However, many of the previous studies were flawed because of low numbers of patients, inadequate data retrieval, or poor controls, and further investigation into this important area is indicated.

The aim of the present study was to quantify the risk of sustaining another low-energy fracture after an index low-energy fracture of the hip, wrist, shoulder, or ankle. This information may be useful in assessments of the reduction in refracture incidence that might be achieved by secondary preventative treatment. It will also help physicians to advise and counsel patients about their future fracture risk and help to justify secondary prophylactic treatment.

Materials and Methods

Our institution is the sole source of adult fracture care for a well-defined local catchment population of 602,897[7]. This population is relatively stable, with an annual migration rate of 0.5%. For the twelve-year period between January 1988 and December 1999, all inpatient and outpatient admissions to our institution due to fracture were audited prospectively. For the purposes of this study, data were collected for patients who were at least forty-five years old, were permanent residents in the catchment area, and had a low-energy fracture of the hip (intracapsular femoral neck or extracapsular intertrochanteric fracture), distal radial metaphysis, proximal humeral metaphysis, or ankle (unimalleolar, bimalleolar, or trimalleolar fracture). Patients with a pathological fracture or a history of high-energy trauma were excluded.

We chose to study fractures of the hip, distal radial metaphysis, proximal humeral metaphysis, and ankle because they are the most commonly seen sites of low-energy fracture in our orthopaedic trauma practice. For the purpose of this study, we considered low-energy index fractures to be those that result from a fall from or below standing height, increase in incidence with age, and occur more often in postmenopausal women. Ankle fractures are bimodally distributed and are not classically considered fragility fractures. However, their incidence is increased in elderly women, and most injuries in these patients are sustained during simple falls[8,9]. Vertebral fractures were not included in this study because they are seen sporadically in our orthopaedic trauma service, and the data set was therefore incomplete.

The patients were allocated to one of nine five-year age cohorts, ranging from individuals between the ages of forty-five and forty-nine years to those at least eighty-five years old. The minimum age of forty-five was chosen because this is the lower end of the 95% confidence interval for the mean age of menopause[10]. It is also the age at which the incidence of fractures sustained during low-energy injury begins to increase dramatically.

All radiographs were individually checked in a prospective manner by the senior authors and were classified according to the zone of injury on admission. Patients who met the study criteria were prospectively assigned a code, which was entered into an SPSS database (version 9; SPSS, Chicago, Illinois). Each patient was identified with a unique hospital number, and this allowed subsequent admissions due to refracture within the twelve-year period to be linked to the index fracture. A random sample of 300 sets of patient records and radiographs were retrieved from the medical records department to estimate the accuracy of our prospective coding system for each of the nineteen data points that were recorded. The mean accuracy was 98.3% (range, 95.6% to 99.7%).

Background demographic data for the catchment area of the unit were obtained from the General Registry Office for Scotland, which has published all census data, including mortality, since 1988. Mortality data for all individuals in the fracture cohort were also obtained from this source by matching the full name, address, and date of birth.

Statistical Analysis

The incidence of refracture in patients with a prior fracture and the incidence of index fracture in the local general population were calculated by dividing the number of fracture events in the cohort during the time-period by the number of person-years of exposure to the risk within the cohort. The person-years at-risk methodology, with censorship at death or at the end of the study, was used to control for the confounding effect of increasing mortality rates with advancing age. The incidence of refracture was divided by the "background" incidence of index fracture within the same local population to calculate the relative risk of refracture in patients who had sustained an index low-energy fracture[11]. This parameter was calculated for all age and sex cohorts and for all possible fracture combinations.

Results

During the twelve-year period of the study, 22,060 patients sustained a total of 22,494 index fractures. The number of index fractures and refractures was greater than the number of patients because some sustained more than one fracture in the same injury. Of these 22,060 patients, 2913 (13.2%) subsequently sustained a total of 3024 refractures during the same period (Table I). During the follow-up period, 6436 patients (29.2%) died, and the median duration of follow-up until either death or the end of the study period was 190 weeks (interquartile range, sixty-seven to 346 weeks; absolute range, one to 624 weeks).

The median ages at the index fracture and refracture

TABLE I Demographic Data on Index Fractures and Refractures

Site of Fracture	No. of Index Fractures			No. of Refractures		
	Men	Women	Total	Men	Women	Total
Hip	1585	6097	7682	159	1160	1319
Wrist	1075	7044	8119	93	861	954
Proximal part of humerus	856	2329	3185	77	443	520
Ankle	1221	2287	3508	39	192	231
Total	4737	17,757	22,494	368	2656	3024

TABLE II Relative Risks (and 95% Confidence Intervals) of Refracture in the Age-Sex Cohorts

Age Cohort *(yr)*	Men	Women	Total
45-49	5.55 (3.66-8.09)	4.94 (3.49-6.78)	5.23 (4.03-6.67)
50-54	6.81 (4.36-10.15)	4.09 (3.19-5.16)	5.14 (4.16-6.29)
55-59	5.65 (3.65-8.36)	3.14 (2.61-3.76)	4.14 (3.50-4.87)
60-64	4.56 (2.74-7.13)	2.93 (2.51-3.40)	3.90 (3.37-4.49)
65-69	6.55 (4.63-9.00)	2.62 (2.27-3.01)	3.62 (3.18-4.11)
70-74	5.96 (4.36-7.95)	2.24 (1.97-2.54)	3.01 (2.68-3.38)
75-79	4.03 (2.85-5.53)	2.20 (1.97-2.44)	2.23 (2.47-3.02)
80-84	3.46 (2.55-4.58)	1.88 (1.71-2.06)	2.23 (2.04-2.43)
≥85	1.23 (0.87-1.69)	1.14 (1.04-1.24)	1.20 (1.10-1.30)
Total	5.55 (4.94-6.21)	2.94 (2.82-3.07)	3.89 (3.73-4.04)

were seventy-four years (interquartile range, sixty-three to eighty-three years) and eighty years (interquartile range, sixty-nine to eighty-six years), respectively. Men had a younger median age than women at both the index fracture (sixty-nine years [interquartile range, fifty-seven to eighty years] compared with seventy-five years [interquartile range, sixty-four to eighty-four years]) and the refracture (seventy-three years [interquartile range, sixty to eighty-two years] compared with eighty years [interquartile range, seventy to eighty-seven years]). The male:female ratio was 1:3.75 for the index fractures and 1:7.22 for the refractures.

The overall relative risk of refracture following an index low-energy fracture was 3.89 (95% confidence interval = 3.73 to 4.04) (Table II). The relative risk was increased for all age-cohorts (Fig. 1) and was higher overall for men (5.55, 95% confidence interval = 4.94 to 6.21) than for women (2.94, 95% confidence interval = 2.82 to 3.07). Younger men (forty-five to seventy-four years of age) appeared to be particularly at risk, whereas the magnitude of risk approached equality for both sexes when the patients were at least eighty-five years of age. The changes in relative risk with age were attributable to the magnitudes of change in the incidences of index fractures and refractures: although both incidences increased with age, the magnitude of increase in index fractures was much greater than that of refractures, resulting in a reduction in relative risk of refracture with advancing age (Fig. 2).

The risk of sustaining a refracture after an index fracture was increased for all combinations of fracture sites studied (Table III), although there was considerable variation in the magnitude of increased risk. Fractures of the hip, wrist, and proximal part of the humerus were associated with a high risk of later refracture at any of the four sites, whereas ankle fractures were associated with a high risk of later ankle fracture

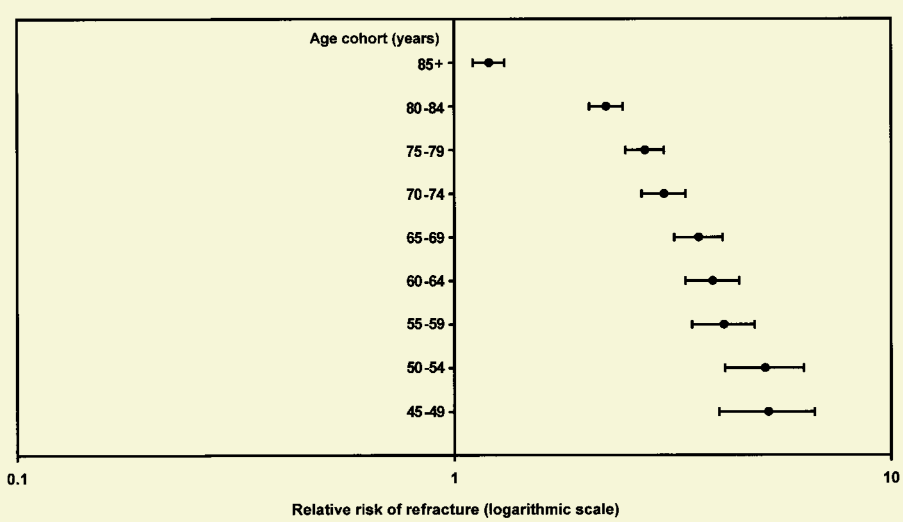

Fig. 1

Relative risk of refracture following the index fracture at any of the four sites studied.

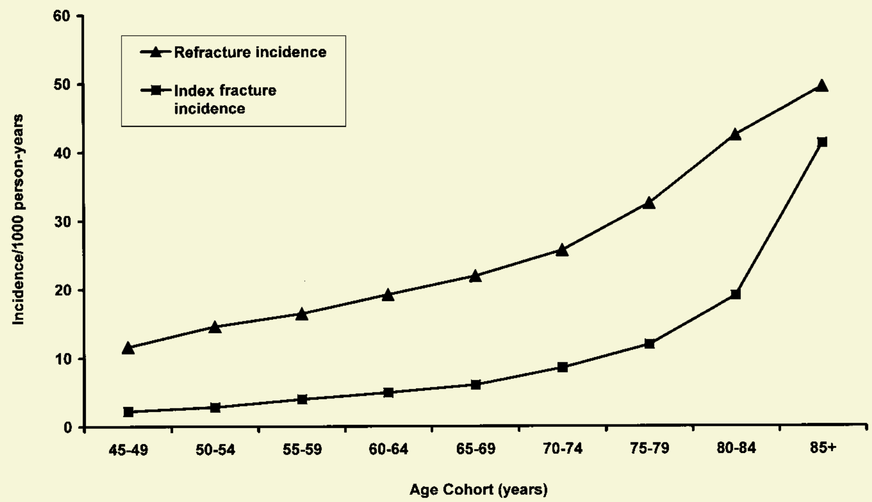

Fig. 2
Incidence of index fracture and refracture in the study population by age cohort.

but a lower risk of fracture at the other three sites. The magnitude of risk was always greatest for a refracture of the same type as the index fracture (relative risk for refracture of the hip, wrist, proximal part of the humerus, and ankle = 9.79, 4.63, 7.91, and 4.53, respectively, following an index fracture at the same site).

Discussion

It is estimated that 40% of postmenopausal women and approximately 25% to 33% of men eventually sustain a fracture, and the incidence of fractures associated with low-energy falls is increasing in the aging population[2,12]. The issue of fracture prevention has therefore never been of greater importance[13,14]. Our study demonstrated that patients who have sustained a low-energy fracture are at increased risk of sustaining another low-energy fracture, when compared with their peers in the same age-sex cohort.

A patient who is at least forty-five years of age and sustains an index fracture of the hip, wrist, proximal part of the humerus, or ankle has an overall relative risk of sustaining a subsequent refracture of any of those types of 3.89 (95% confidence interval = 3.73 to 4.04) compared with the "background" incidence of index fractures. These results are consistent with those of other studies in which a previous fracture was examined as a risk factor for refracture[15-18], but they suggest that the influence is actually greater than was formerly estimated. For example, the relative risk of a hip fracture following a wrist fracture has been reported to range between 1.4 and 2.7 in the literature[19-21], whereas we found a substantially greater relative risk of 3.22 (95% confidence interval = 2.81 to 3.66).

The reason for the differences between our relative risk estimates and those in other studies is difficult to appraise. Many of the previous studies were cross-sectional mail surveys or case-control studies or were performed retrospectively by a review of case records, which may have underestimated the risk. To our knowledge, ours is the first prospective cohort study using a person-years at-risk methodology, which adjusts for the effects of mortality in reducing the time that elderly individuals are at risk. Because the study was population-based, there was no selection bias and the patients in the control group were from the same population. The accuracy of our

TABLE III Relative Risks (and 95% Confidence Intervals) of Refracture According to Fracture Location

	Index Fracture				
Refracture	Hip	Wrist	Proximal Part of Humerus	Ankle	Any
Hip	9.79 (9.07-10.55)	3.22 (2.81-3.66)	5.76 (4.94-6.68)	1.30 (0.95-1.82)	6.55 (6.17-6.94)
Wrist	3.96 (3.59-4.36)	4.63 (4.22-5.06)	4.42 (3.83-5.08)	2.03 (1.62-2.51)	4.04 (3.79-4.29)
Proximal part of humerus	6.50 (5.72-7.38)	4.08 (3.46-4.79)	7.91 (6.59-9.42)	1.96 (1.32-2.81)	5.23 (4.77-5.72)
Ankle	1.74 (1.34-2.18)	2.23 (1.81-2.74)	2.20 (1.57-2.99)	4.53 (3.57-5.66)	2.41 (2.12-2.72)
Any	5.76 (5.32-6.17)	3.98 (3.52-4.42)	4.87 (4.27-5.47)	2.24 (1.89-2.59)	3.89 (3.73-4.04)

data recording, confirmed by a retrospective evaluation of 300 records, indicates that large systematic errors are unlikely.

Men were found to be at higher risk than women, with relative risks of sustaining any refracture after any index fracture of 5.55 and 2.94, respectively. This may be explained by the incidence of index fracture in the local population: it was higher in women, so the proportional increase in the relative risk of refracture after an index fracture was smaller in women[22]. It is also possible that greater alcohol intake among middle-aged men who sustain fractures could have contributed to their increased risk of refracture[23] because the deleterious effects of alcohol include an increased risk of falls and a premature reduction in bone mass[24-26].

The relative risk of refracture was increased for every combination of fracture and refracture in the younger patients, and it decreased progressively with advancing age. With increasing age, the incidence of index fracture in the local general population increased at a greater rate than did the incidence of refracture in the fracture cohort. As a result, the relative risk of sustaining a subsequent fracture after the index fracture decreased with age, to an extent that, by the age of eighty-five years, it was little more than that of the local general population. Even though this cohort of very elderly individuals has the highest incidence of refractures, their relative risk for refracture is little more than that of individuals in their age-sex cohort, so they do not represent an especially high-risk group. Thus, it appears that little advantage would be gained from commencing secondary preventative treatment on the basis of a previous fracture alone in the age-group of eighty-five years of age and older.

Younger individuals had a lower incidence of refracture following an index fracture but a higher relative risk. This risk is also likely to be present over a longer period because of the greater life expectancy of these individuals. Targeting secondary preventative strategies to these younger individuals following an initial low-energy fracture is likely to be more effective. For example, treatment of osteoporosis in patients of this age has been shown to decrease fracture incidence[27], although at present few receive relevant counseling or treatment[14,28].

A primary aim of public-health measures is to prevent hip fractures. These common fractures are associated with a high mortality rate, of up to 35% at one year[29], and more than half of the survivors never regain their prefracture level of walking[30-32]. Prevention of these fractures is also important from an economic viewpoint, as most patients require inpatient surgical treatment and many subsequently need increased costly community care. The relative risk of a hip refracture following a hip, wrist, proximal humeral, or ankle fracture was 9.79, 3.22, 5.76, and 1.30, respectively. Fractures of the hip, wrist, and proximal part of the humerus are all therefore associated with an increased risk of later hip fracture. By identifying the subgroups that are at an increased risk of sustaining a hip fracture, the results of this study suggest that secondary preventative strategies targeted specifically to these individuals may be more productive than targeting the entire population with osteoporosis, which comprises more than a third of women over sixty years of age.

Our study identified some of the factors associated with an increased risk of refracture, although we were unable to examine the effects of other important factors such as severity of osteoporosis, genetic factors, medical comorbidities and their treatment, and alcohol and tobacco abuse. Prospective evaluation of these factors in a longitudinal cohort study may allow a greater degree of sensitivity in predicting the risk of refracture following an index low-energy fracture.

In conclusion, a low-energy fracture presents a greater risk than has previously been appreciated of sustaining a second low-energy fracture later in life. The younger the patient at the time of the index fracture, the greater his or her relative risk of refracture. Thus, aggressive secondary preventative measures are indicated for younger patients who sustain a first low-energy fracture. Such interventions should be in the form of medical investigation and treatment of low bone-mineral density and modification of other risk factors for fracture. ■

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