

Progressively Increasing Fracture Risk With Advancing Age After Initial Incident Fragility Fracture: The Tromsø Study

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ABSTRACT

The risk of subsequent fracture is increased after initial fractures; however, proper understanding of its magnitude is lacking. This population-based study examines the subsequent fracture risk in women and men by age and type of initial incident fracture. All incident nonvertebral fractures between 1994 and 2009 were registered in 27,158 participants in the Tromsø Study, Norway. The analysis included 3108 subjects with an initial incident fracture after the age of 49 years. Subsequent fracture ($n = 664$) risk was expressed as rate ratios (RR) and absolute proportions irrespective of death. The rates of both initial and subsequent fractures increased with age, the latter with the steepest curve. Compared with initial incident fracture rate of 30.8 per 1000 in women and 12.9 per 1000 in men, the overall age-adjusted RR of subsequent fracture was 1.3 (95% CI, 1.2–1.5) in women, and 2.0 (95% CI, 1.6–2.4) in men. Although the RRs decreased with age, the absolute proportions of those with initial fracture who suffered a subsequent fracture increased with age; from 9% to 30% in women and from 10% to 26% in men, between the age groups 50–59 to 80+ years. The type of subsequent fracture varied by age from mostly minor fractures in the youngest to hip or other major fractures in the oldest age groups, irrespective of type and severity of initial fracture. In women and men, 45% and 38% of the subsequent hip or other major fractures, respectively, were preceded by initial minor fractures. The risk of subsequent fracture is high in all age groups. At older age, severe subsequent fracture types follow both clinically severe and minor initial incident fractures. Any fragility fracture in the elderly reflects the need for specific osteoporosis management to reduce further fracture risk. © 2013 American Society for Bone and Mineral Research.

KEY WORDS: FRACTURE; OSTEOPOROTIC FRACTURE; SUBSEQUENT FRACTURE; POPULATION-BASED STUDY

Introduction

Declining age-specific rates of hip fractures are reported in Western countries.^(1–5) Nevertheless, with an increasing aging population, osteoporotic fractures, notably those of the

hip, vertebra, and distal forearm, represent a major public health problem.⁽⁶⁾ After any type of low-trauma fracture, there is an increased risk of a subsequent fracture.⁽⁷⁾ Although the latter may be elevated to more than twofold for combinations of hip, vertebra, wrist, and any site,^(8–14) there is a view that the

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competing risk of death obviates this risk in older individuals, leading to reluctance to initiate treatment with effective therapies.

There is also debate concerning the strength of the relation between the various sites of initial fractures: forearm,^(14–17) hip,^(18–22) ankle,⁽²³⁾ or rib,⁽²⁴⁾ and subsequent fracture risk. Some studies have reported higher risk in men,^(12,15,25,26) particularly in men with an initial wrist⁽¹³⁾ or ankle fracture,⁽⁷⁾ whereas no gender differences are reported by others.^(9,10,27) Risk of subsequent fracture may also vary by age,⁽¹⁷⁾ with different age-effects depending on location of the initial fracture. Generally, relatively small cohort size, short follow-up, and lack of comprehensive fracture registration limit inferences from many previous studies. Moreover, the effect of age, sex, and site of initial fracture on type of subsequent fracture is not well described. To enhance clinical decision making, algorithms or models for estimation of fracture probability have been developed on basis of clinical risk factors, among them prior fragility fracture.^(28–31) These models use history of prior fragility fracture, asking for a yes/no response without consideration of fracture location, severity of fracture, time since fracture, or how possible gender differences may influence the association between prior and subsequent fracture risk.^(32,33)

The aim of this study was to improve our understanding of subsequent fracture risk by examining: (1) incidence rates and rate ratios (RR) of subsequent fracture by sex, age, and type or location of initial fracture; (2) the burden of subsequent fractures irrespective of the risk of death; and (3) the relation between different types of subsequent and initial fracture.

Subjects and Methods

Study population

The Tromsø Study is a population-based health study in the municipality of Tromsø in Northern Norway. Six surveys have been conducted from 1974 to 2008.⁽³⁴⁾ This analysis uses data from the 1994–95 survey to which all residents born in 1969 or earlier ($n = 37,558$) were invited and 27,158 (72%) participated. Among these, 245 (0.9%) subjects withdrew from the study or moved before the study started, and 26 (0.1%) subjects who suffered pathological fractures were excluded. Thus 26,887 subjects were eligible for the analyses. The Regional Committee of Medical Research Ethics and the Norwegian Data Inspectorate approved the study. All participants gave written informed consent.

Fracture registration

The fracture registry covered the 15-year period from the date of examination at the fourth survey (1994–95) through December 31, 2009, with respect to all nonvertebral fractures. Vertebral fractures were excluded because date of occurrence was usually not reliable. The fracture registry is based on the radiological archives at the University Hospital of North Norway in Tromsø. The nearest alternative radiology service or fracture treatment facility is located 250 km from Tromsø. The only fractures that would be missed are those, for which no radiology was

performed or where such investigations occurred while the subject was travelling and for which no local follow-up was performed. The computerized records in the radiological archives of the University Hospital contain the national personal identification number, which is unique for each resident of Norway, time of investigation, fracture codes, and descriptions. All abnormal radiological examinations were reviewed to ascertain the fracture code, to identify exact fracture type and anatomical location, to distinguish consecutive fracture occasions in the same person, and to capture fractures that had not been coded correctly as fractures. In addition, the hospital discharge records were checked with respect to hip fractures. A similar registration has previously been described and validated.⁽³⁵⁾

Statistical analyses

Incidence rates (per 1000 person-years) were calculated by dividing the total number of new fractures by the sum of person-years during the follow-up period. We calculated the rate of initial fracture in subjects who were 50 years or older at the date they attended the survey ($n = 10,236$). For any nonvertebral initial fracture ($n = 3108$), follow-up time was calculated from the date of examination (during 1994–95) to the date of first fracture or censoring (migration, death, or December 31, 2009).

The calculation of nonvertebral subsequent fracture rate was restricted to subjects who suffered their initial fracture from the age of 50 years or older. For any nonvertebral subsequent fracture, follow-up was calculated as the time between the first and the next fracture or until censoring.

Rate ratios (RRs) and 95% confidence intervals (CIs) were calculated by comparing age-adjusted incidence rates of subsequent fracture with age-adjusted rates of initial fracture based on Poisson assumptions. Incidence rates and RRs of subsequent fracture were also calculated according to initial fracture location and age at initial fracture. Initial fractures were classified into hip, major (proximal humerus, pelvis, distal femur, and proximal tibia), and minor (all other sites except skull and vertebrae). Age at initial fracture was grouped as 50–59, 60–69, 70–79, and ≥ 80 years. Tests of interaction were performed to determine any differential effects of gender and age groups on the RRs.

In the oldest age groups, a substantial proportion died during follow-up. To estimate the burden of fractures, the proportions of all participants with an initial fracture who also suffered a subsequent fracture were calculated. The proportions were estimated within the first 5 years of follow-up from date of initial fracture. To ensure a 5-year follow-up in all subjects, only those with initial fracture before 2005 were included. For comparison, the percentages of women and men who suffered an initial incident fracture within the first 5 years of follow-up after the fourth survey were also calculated.

All analyses were performed using the SAS statistical package, v9.2 (SAS Institute Inc., Cary, NC, USA) and STATA 12.0 (StataCorp. 2011. Stata Statistical Software: Release 12; StataCorp LP, College Station, TX, USA). The criterion for statistical significance was set at $p < 0.05$.

Results

For subjects who were 50 years or older at the 1994–95 survey ($n = 10,236$), the overall rate of initial incident fracture per 1000 person-years was 30.8 (95% CI, 29.4–32.3) in 5429 women and 12.9 (95% CI, 12.0–14.0) in 4807 men. The mean age at initial fracture was 72.9 (SD = 10.1) in women and 70.9 (SD = 10.4) in men. During follow-up, 2156 women and 952 men suffered an initial incident fracture after the age of 50 years. Among those, 536 women and 128 men suffered a subsequent fracture before the end of follow-up. The median follow-up time from initial to subsequent fracture or censoring was 4.0 years in women (interquartile range [IQR], 1.6–7.5 years) and 3.7 years (IQR 1.3–7.2 years) in men. The mean age at subsequent fracture was 75.3 (SD = 11.0) in women and 70.7 (SD = 11.3) in men.

The overall age- and sex-adjusted RR of subsequent fracture after any initial incident fracture was 1.4 (95% CI, 1.3–1.6). There

was a significant differential effect of gender (p value for interaction was <0.001) on RR after any initial fracture. Similar interactions with gender were also found with RRs after initial hip ($p = 0.003$), major ($p = 0.012$), and minor fractures ($p = 0.047$). There were no significant interactions with age groups (except for RR after major fracture, $p = 0.006$); however, the results are presented stratified by age groups to show the sex-specific and age group-specific ratios.

The RRs of subsequent fractures by initial fracture type and age of initial incident fracture and gender are presented in Table 1. In women, the overall age-adjusted RR of subsequent fracture after any type of initial fracture was 1.3 (95% CI, 1.2–1.5) and after initial hip, major, and minor fracture the RRs were 1.6 (95% CI, 1.3–1.9), 1.6 (95% CI, 1.3–1.9), and 1.3 (95% CI, 1.2–1.5), respectively. After other types of initial fracture, the RRs varied between 1.2 (95% CI, 0.9–1.6) after initial hand fracture and 1.5 (95% CI, 1.1–2.1) after initial foot fracture. In men, the overall RR of

Table 1. Rate Ratios (95% CI) of Subsequent Fractures by Initial Fracture Type/Location and Age at Initial Fracture in Women and Men

Initial fracture type	Initial/subsequent (n)	Overall (≥ 50 years)	50–59 years	60–69 years	70–79 years	≥ 80 years
Women						
Any	2156/536	1.3 (1.2–1.5)	1.7 (1.4–2.1)	1.2 (1.0–1.5)	1.3 (1.1–1.5)	1.3 (1.0–1.6)
Hip	526/147	1.6 (1.3–1.9)	2.9 (1.4–5.8)	1.6 (0.9–2.8)	1.4 (1.0–1.8)	1.7 (1.3–2.2)
Major ^a	429/124	1.6 (1.3–1.9)	2.5 (1.5–4.2)	1.7 (1.1–2.6)	1.4 (1.0–1.9)	1.5 (1.1–2.2)
Minor ^b	1557/370	1.3 (1.2–1.5)	1.6 (1.3–2.0)	1.2 (0.9–1.5)	1.3 (1.1–1.6)	1.2 (0.9–1.5)
Upper limb ^c	1296/320	1.3 (1.2–1.5)	1.8 (1.4–2.3)	1.2 (0.9–1.5)	1.3 (1.0–1.6)	1.1 (0.8–1.5)
Shoulder	276/75	1.4 (1.1–1.8)	2.6 (1.4–4.7)	1.4 (0.8–2.4)	1.3 (0.9–1.9)	1.2 (0.8–1.8)
Wrist	873/220	1.3 (1.2–1.5)	1.9 (1.5–2.5)	1.2 (0.9–1.5)	1.3 (1.0–1.7)	1.1 (0.7–1.6)
Hand ^d	196/42	1.2 (0.9–1.6)	2.1 (1.2–3.5)	1.0 (0.6–1.8)	1.2 (0.6–2.3)	0.7 (0.3–1.6)
Lower limb ^e	637/153	1.5 (1.3–1.8)	1.5 (1.0–2.1)	1.7 (1.3–2.4)	1.4 (1.0–1.8)	1.7 (1.2–2.5)
Ankle	302/66	1.3 (1.0–1.7)	1.7 (1.0–2.7)	1.4 (0.9–2.2)	1.2 (0.8–1.8)	1.1 (0.5–2.1)
Foot ^f	166/35	1.5 (1.1–2.1)	1.0 (0.5–1.9)	2.2 (1.3–3.8)	1.2 (0.6–2.8)	2.1 (1.0–4.6)
Men						
Any	952/128	2.0 (1.6–2.4)	2.0 (1.4–2.7)	2.1 (1.4–3.1)	2.0 (1.4–2.9)	1.4 (0.9–2.3)
Hip	228/38	2.8 (2.0–3.9)	2.5 (0.8–7.8)	4.9 (2.4–9.8)	2.6 (1.5–4.6)	1.7 (0.9–3.1)
Major ^a	130/24	2.8 (1.9–4.2)	4.7 (2.4–9.2)	3.5 (1.6–8.0)	2.5 (1.0–6.0)	1.1 (0.4–3.1)
Minor ^b	665/79	1.7 (1.3–2.1)	1.7 (1.2–2.4)	1.7 (1.1–2.7)	2.0 (1.3–3.1)	1.0 (0.5–2.2)
Upper limb ^c	417/51	1.8 (1.4–2.4)	1.7 (1.0–2.7)	1.8 (1.0–3.2)	2.3 (1.3–3.9)	1.3 (0.6–2.9)
Shoulder	72/12	2.9 (1.6–5.1)	3.0 (1.0–9.3)	2.7 (0.7–10.8)	2.7 (1.0–7.4)	2.7 (0.8–8.7)
Wrist	151/16	1.4 (0.9–2.4)	0.9 (0.3–2.8)	2.1 (0.9–4.7)	1.9 (0.8–4.7)	0.7 (0.2–3.1)
Hand ^d	186/22	1.8 (1.2–2.8)	1.9 (1.0–3.5)	1.1 (0.4–3.3)	2.9 (1.3–6.5)	1.2 (0.3–5.0)
Lower limb ^e	322/46	2.0 (1.5–2.7)	2.6 (1.7–4.0)	2.3 (1.3–4.1)	1.5 (0.8–3.0)	0.9 (0.3–2.5)
Ankle	144/24	2.5 (1.7–3.7)	2.2 (1.1–4.4)	2.7 (1.3–5.8)	2.4 (1.1–5.4)	3.0 (0.9–9.6)
Foot ^f	105/12	1.7 (1.0–3.0)	1.8 (0.8–4.1)	2.7 (1.0–7.3)	1.0 (0.2–4.0)	0/2 ^g

Values are number of fractures (n) or rate ratios (95% CI). Rate ratios are age-adjusted, and are based on subsequent fracture rates divided by the following initial fracture rates (according to age category and sex): All (50+ years): 30.8/1000 for women and 12.9/1000 for men; 50–59 years: 19.5/1000 for women and 9.8/1000 for men; 60–69 years: 31.8/1000 for women and 11.9/1000 for men; 70–79 years: 48.1/1000 for women and 21.9/1000 for men; ≥ 80 years: 71.9/1000 for women and 43.7/1000 for men.

CI = confidence interval.

^aMajor included: proximal humerus, pelvis, distal femur, and proximal tibia.

^bMinor included: all other types except hip, skull, and vertebrae.

^cUpper limb included: humerus, radius, ulna, and hand bones.

^dHand included: carpal, metacarpal, and finger bones.

^eLower limb included: femur (except hip), knee, tibia, fibula and foot bones.

^fFoot included: tarsal, metatarsal and toe bones.

^gNo subsequent fracture in 2 subjects with initial foot fractures.

subsequent fracture was 2.0 (95% CI, 1.6–2.4), and the RRs were 2.8 (95% CI, 2.0–3.9), 2.8 (95% CI, 1.9–4.2), and 1.7 (95% CI, 1.3–2.1) after initial hip, major, and minor fracture, respectively. After other specific types of initial fracture, the RRs varied between 1.4 (95% CI, 0.9–2.4) after initial wrist fracture and 2.9 (95% CI, 1.6–5.1) after initial shoulder fracture. In women, the highest risk of subsequent fracture was observed in the age group 50–59 years, with RRs of 2.9 (95% CI, 1.4–1.9) and 2.5 (95% CI, 1.5–4.2) after initial hip and major fracture, respectively. The highest risk of subsequent fracture in men was observed after initial hip fracture in the age group 60–69 years (RR, 4.9; 95% CI, 2.4–9.8), and after initial major fracture in the age group 50–59 years (RR, 4.7; 95% CI, 2.4–9.2).

The incidence rates (per 1000 person-years) of initial incident fracture of any type increased with age in both sexes (Fig. 1). For initial major and minor fractures in general, although they increased with age (except minor fracture in men), the rates of increase were less than those for initial hip fracture. On the other hand, the incidence rates of subsequent fractures of any type were higher than the incidence rates of initial fracture, irrespective of the type of initial fracture, across all age groups (Fig. 1). Moreover, these rates increased substantially with age in both sexes. After initial fracture of any type in women, the rates increased from 30/1000 person-years in the age group 50–59 years to 97/1000 person-years in the age group 80+ years. In men these rates increased from 17 to 63/1000 person-years for the corresponding age groups. These rates were especially high after initial hip and/or major fracture in the age groups above

70 years. Excluding subjects with self-reported previous fractures after the age of 50 years, but before 1994–95 ($n = 400$) did not change the estimates of rates or proportions.

The proportion of participants with a subsequent fracture also increased progressively with advancing age irrespective of censoring (Fig. 2). The proportion of subjects who suffered a subsequent fracture was higher than those who suffered an initial fracture within a similar follow-up period (shaded area in Fig. 2), and this was evident in the older subjects irrespective of censoring, particularly in women. A substantial proportion of the subsequent fractures occurred during the first 5 years after initial fracture. The percentages of women who had a subsequent fracture within the first 5 years after an initial fracture of any type rose from 13% in the age group 50–59 to 24% in the age group above 80 years. The corresponding figures in men were from 10% to 18%. The same age-related pattern of increasing subsequent fracture proportions was observed after initial hip, major, and minor fractures in women. In men the highest proportions of subsequent fracture occurred in those younger than 70 years after initial hip and major fractures, and in those older than 70 years after initial minor fracture. In a sensitivity analysis taking into account the competing risk of death, the 5-year cumulative incidence of subsequent fracture also increased with advancing age in women from 7% to 21% in the youngest age group to 28% to 32% in the oldest age group, after the different initial fracture locations or types. In men, the 5-year cumulative incidence—similar to the proportions who suffered subsequent fracture—was highest in the age groups: 60–69

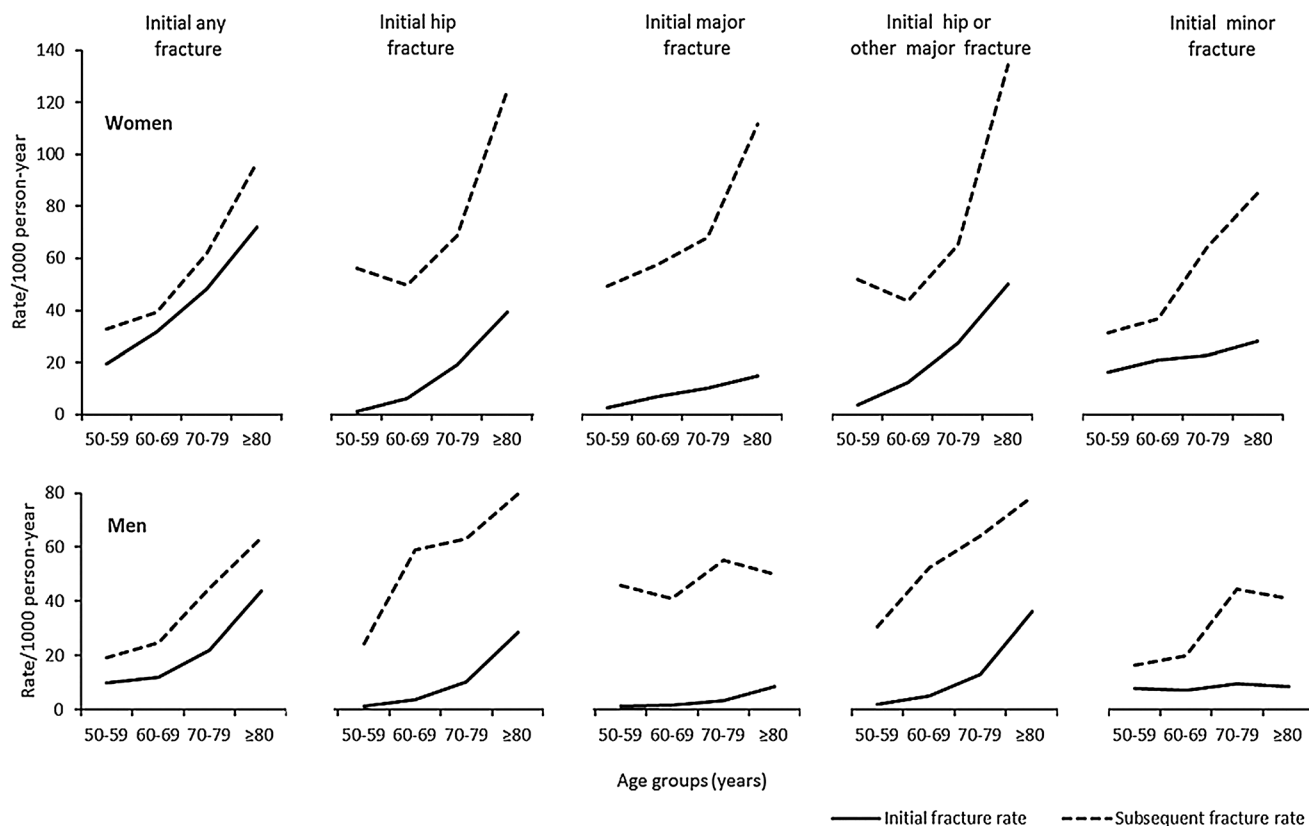
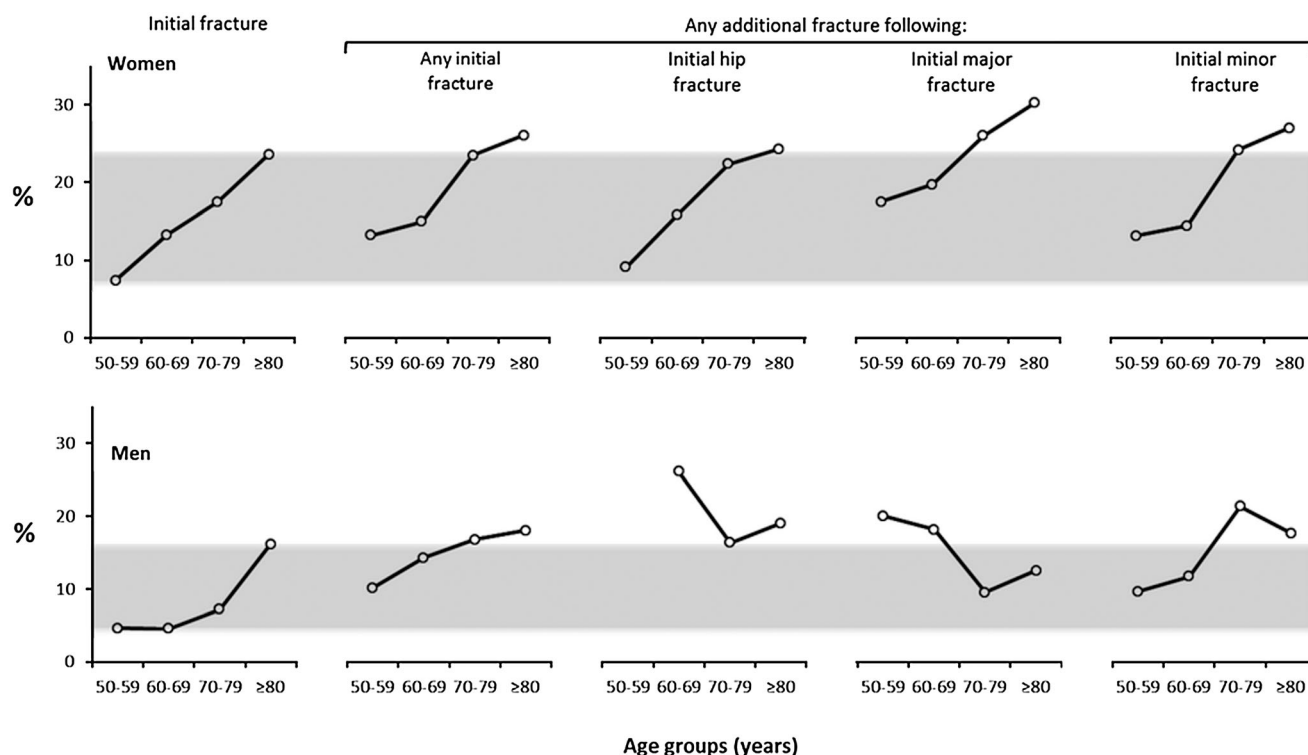


Fig. 1. Incidence rates of initial and subsequent fractures by type and age at initial fracture in women and men.



The shaded area represents the percentages of initial fracture within the first 5 years of follow-up.

Fig. 2. Percentages of participants with an initial fracture and with a subsequent fracture within 5 years after the initial fracture, according to initial fracture type and by age groups at initial fracture in women and men.

years after initial hip fracture (19%), 50–59 years after initial major fracture (21%), and 70–79 years after initial minor fracture (20%); however, the cumulative incidence remained high (13% to 16%) in the oldest age group after the different locations/types of initial fracture.

Increasing risk of hip and other major fractures was noted with advancing age irrespective of the initial fracture location with similar patterns in women and men (Fig. 3). Initial minor, major, and hip fractures were mostly followed by subsequent hip or other major fractures in the older age groups and by minor fractures in the youngest age groups. Initial hip and other major fractures were combined because the patterns of subsequent fracture after those fractures were indistinguishable. In both sexes, 11% to 12% of the subsequent fractures were hip or other major after initial minor fractures in the age group 50–59 years. This increased to 64% in women and 43% in men in the oldest age group. After initial hip or other major fractures, 13% to 14% of the subsequent fractures were hip or other major in the youngest age group. This increased to 65% in women and 84% in men in the oldest age group. Of subjects with subsequent hip or other major fractures, 45% of women and 38% of men were preceded by an initial minor fracture.

Discussion

This large cohort showed increasing risk of both initial incident and subsequent fractures with age in women and men 50 years and older. The absolute proportions of those with initial incident fracture who suffered a subsequent fracture also increased with

age, and were already high the first few years after the initial fracture. Importantly, the risk of subsequent fracture was elevated over and above the risk of initial fracture across age groups. In the youngest, any type of initial fracture was mostly followed by a minor fracture, whereas in the oldest it was followed by a hip or other major fracture. Although minor fractures are considered less serious, they comprised a large proportion of all fractures and were associated with increased risk of subsequent fracture, and in the oldest they were followed by the more clinically serious hip or other major fractures.

Differences in risks estimates between studies could be related to differences in study populations, methods of fracture ascertainment, types and locations of fractures, or duration of follow-up,^(7,9) as well as on calculation methods: RRs, hazard ratios (HRs), or standardized incidence rates. This study presents subsequent nonvertebral fracture risk after different types of initial nonvertebral fractures in a large cohort of women and men over a wide age range. The subsequent fracture risk is reported as the rate ratio between the age-adjusted subsequent fracture rate and the rates of the initial fracture, and age group allocation were according to age at initial fracture.

Although covering a wider age range, the overall age-adjusted RR of a subsequent fracture of 1.3 in women and 2.0 in men in the present study was similar to those reported by others.^(8,9,12,14) The RRs of subsequent fractures were significantly increased across all age groups, but highest in those with initial fracture before the age of 70 years, as also observed by others.⁽⁹⁾ The overall RRs of subsequent fracture in women and men after initial hip fracture were comparable to previously reported risks,^(7,14)

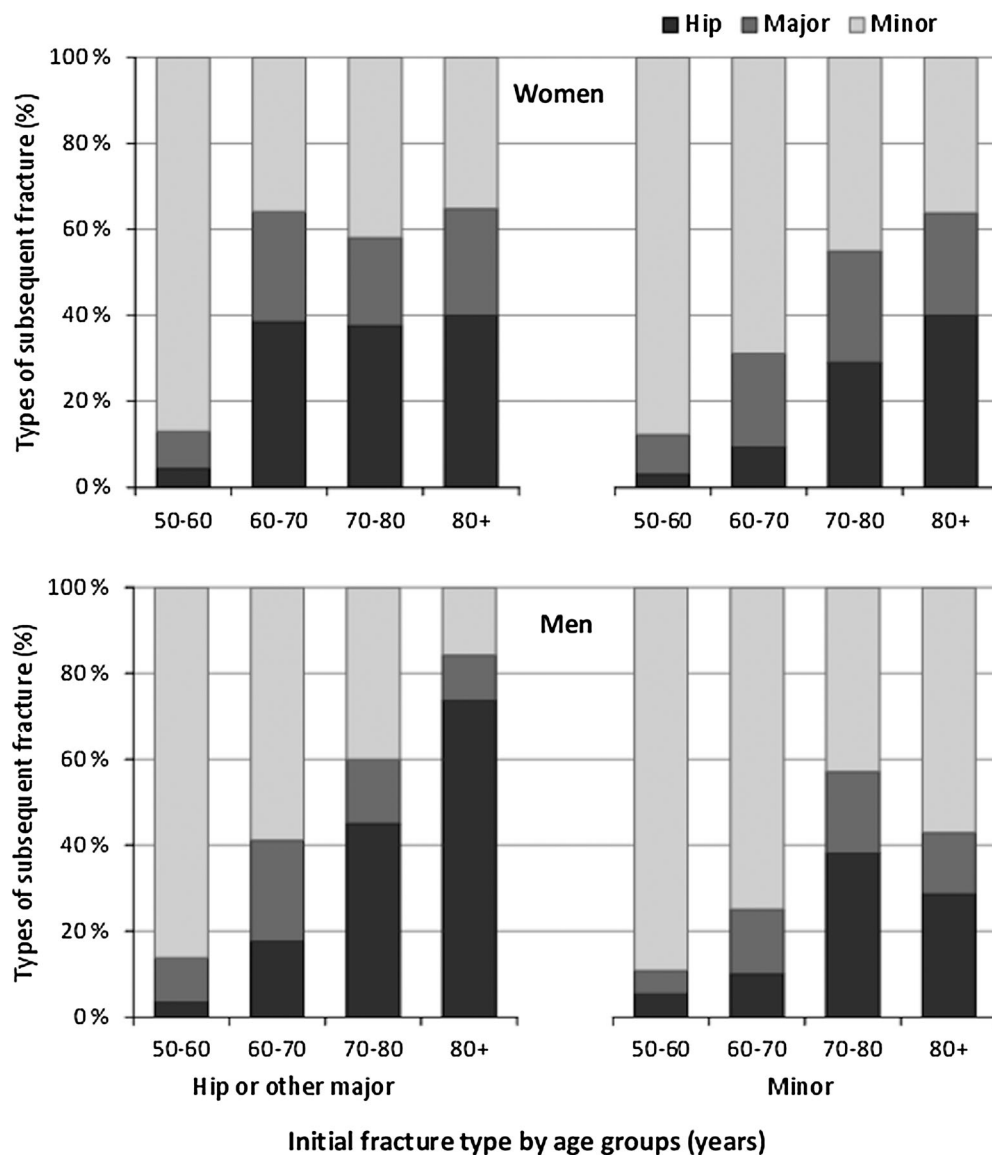


Fig. 3. Distribution of types of subsequent fractures by types and age of initial fracture in women and men.

taking into account differences in age groups and adjustments. The risk of subsequent fracture was also high after initial major fracture. This elevated risk was, to a large extent, explained by the increased risk after humeral fractures, the most common among major fractures; 64% in women and 55% in men (Table 1). The nearly twofold increased risk after humerus fracture corresponds to the elevated risk reported in women above 45 years, albeit after adjustment for bone mineral density.⁽¹⁴⁾

This study highlights the elevated risk of subsequent fracture after minor fractures. Few data exist on subsequent fracture risk after minor fractures, and discrepancies between existing studies indicate a great need for further studies that also include details on the locations of minor fractures. In a recently published study, minor fractures were a significant predictor of subsequent fracture in women above 45 years of age (HR, 1.45; 95% CI, 1.13–1.87).⁽¹¹⁾ This is not easily comparable to our study, because of different categorization of fractures; forearm fractures were defined as major fractures.⁽¹¹⁾ Nonetheless, in the present study initial wrist fractures represented a large proportion of the minor

fractures in women. After initial forearm fractures, the overall RR of any subsequent fracture was 1.3 in women and 1.4 in men, comparable to those reported by Hodsman and colleagues,⁽¹⁴⁾ but slightly lower than the adjusted rates reported by Barrett-Connor and colleagues.⁽¹⁷⁾ More important, the findings from this study indicate that minor fractures after the age of 50 years are important signals of future hip or other major fractures, because 45% and 38% of the subsequent hip or other major fractures were preceded by initial minor fractures in women and men, respectively.

The RRs of subsequent fracture observed in the present study are comparable to earlier reports.⁽¹⁹⁾ Although greater than 1.0 across the age groups irrespective of initial fracture types, the RRs of subsequent fractures tended to decrease with age. This does not indicate a decreasing subsequent fracture risk with increasing age. On the contrary, the rates of subsequent fractures increased progressively with age. Therefore, the age-related increases in subsequent fracture risk are not truly reflected in the RRs. Expressing the risk of subsequent fracture in

terms of RR is misleading in the older age groups, because the relative age-related decline in RR is due to the rising underlying risk of initial fracture, and is observed in spite of an increasing absolute subsequent fracture risk. Moreover, in this study the RRs were based on the overall rates of any initial fracture, which are already high in this population. Nevertheless, if the RRs were based on the type-specific initial fracture rates, they indicate a threefold to sevenfold increased risk of subsequent fracture after initial hip or major fracture in both women and men aged 80 years or older.

Most importantly, this study explores the risk of subsequent fracture irrespective of the risk of death. Although low-trauma fractures are associated with an increased risk of death,⁽³⁶⁾ the proportion of people with subsequent fracture increases with age despite this competing risk. Among those with any initial fracture after the age of 80 years, 26% of women and 18% of men suffered a subsequent fracture regardless of their high risk of death. In women, the proportions were similarly high even after initial hip or other major fracture. Moreover, similar patterns of increased subsequent fracture risk with age were also found when the competing risk of death was taken into account. In men, the cumulative incidences from the competing risk models were generally lower than the absolute proportions of those who suffered subsequent fracture due to the increased risk of death. However, although the risk of subsequent fracture was highest in men younger than 70 years, it remained relatively high (13% to 16%) in those older than 70 years despite the increased mortality after initial hip or other major fractures.

As shown by others,⁽⁷⁾ the elevated risk of subsequent fracture was especially high during the first years after initial fracture, which indicate a very critical period directly after the initial fracture, particularly in the oldest age group. Treatment within 90 days after hip fracture have been shown to reduce the rate of new fractures,⁽³⁷⁾ and evidence for effective prevention of subsequent fracture has been reported recently.⁽³⁸⁾ Our findings indicate that the absolute risk of subsequent fractures increases with age even following those who survive after initial hip or other major fractures. Moreover, age largely determines the type and seriousness of subsequent fracture. The imperative to treat increases with age as the risk of more serious fractures increases with advancing age after any prior fracture location or type. Therefore, older subjects with prior fragility fracture represent an important target for specific osteoporosis management to reduce the risk of new fractures and potentially premature mortality.

Strengths of the study include the prospective population-based design with a long follow-up period in a large cohort of women and men across a wide age span, with a validated fracture registry of all nonvertebral fractures occurring in the cohort. This gave the opportunity to compare risk of subsequent fractures across age groups and to study in detail the types of subsequent fractures that follow different locations of initial fractures. A limitation of the study is the lack of vertebral fracture registration. As in most epidemiologic studies, there is uncertainty about the degree of trauma associated with the fracture event. However, a subgroup analysis (including 484 and 307 subjects with confirmed low-trauma and high-trauma fractures, respectively) indicated that the incidence rates of subsequent fractures were similar in women independent of the

energy involved, and slightly higher in men after an initial low-energy fracture (data not shown).

In summary, this study shows that the absolute risk of subsequent fracture increases with age irrespective of the competing risk of death, and after all types of initial fracture, including minor fractures. In the elderly, minor fractures signal an increased risk of the more serious hip or other major fractures. Any fragility fracture in the elderly reflects the need for specific osteoporosis management to reduce further fracture risk and potentially premature mortality; indeed, despite the competing risk of early death.

Disclosures

All authors state that they have no conflicts of interest.

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