The Impact of Nonhip Nonvertebral Fractures in Elderly Women and Men

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Context: Nonhip nonvertebral fractures represent half of all osteoporotic fractures; however, their contribution to the burden of refracture and premature mortality is unclear.

Objectives: To examine the risk and burden of subsequent fracture and mortality associated with an initial nonhip nonvertebral fracture.

Setting and Participants: This is a prospective cohort from the Dubbo Osteoporosis Epidemiology Study, 1989–2010 of community dwelling participants aged 60+ with incident fractures.

Outcome Measures: Relative risk of all subsequent fractures and age-adjusted standardized mortality ratios were calculated according to initial fracture type. The total burden of adverse events was assessed using competing risk models with four potential outcomes: mortality after initial fracture, mortality after subsequent fracture, subsequent fracture and alive, or event-free.

Results: Of the 952 fractures in women and 343 in men, over half were nonhip nonvertebral fractures (486 in women and 173 in men). Nonhip nonvertebral fractures were associated with increased risk of any subsequent fracture (1.95 [1.67–2.27] for women and 2.47 [1.82–3.35] for men), hip refracture (2.11 [1.04–4.28] for women and 2.63 [1.35–5.13] for men), and vertebral refracture (1.89 [1.43–2.48] for women and 2.13 [1.20–3.79] for men). More importantly, nonhip nonvertebral fractures were associated overall with 20% excess mortality for the first 5 years postfracture, of which approximately half were due to initial fracture and the remaining due to subsequent fractures. Proximal fractures were associated with increased mortality risk per se, whereas distal fractures were associated with increased mortality risk only in the group who sustained subsequent fractures.

Conclusion: Nonhip nonvertebral fractures are associated with significant risk of subsequent fracture including hip and vertebral refracture, and premature mortality. Due to their high prevalence, about half of all subsequent fractures and a quarter of all fracture-related excess mortality were attributable to nonhip nonvertebral fracture. Thus nonhip nonvertebral fracture warrants early investigation and appropriate intervention. **(*J Clin Endocrinol Metab* 99: 415–423, 2014)**

Nonhip nonvertebral (NHNV) fractures make up approximately 50% of all clinical fractures yet receive far less attention than either hip or vertebral fractures. This is partly due to the preconceived notion that serious adverse effects after a fracture, such as premature mortality, increased morbidity, and high community costs, are primarily related to hip and vertebral fractures. In addition, certain types of NHNV fractures, such as ankle fractures, are not thought to be osteoporotic fractures (1–3).

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Abbreviations: CI, confidence interval; NHNV, nonhip nonvertebral; SMR, standardized mortality ratios; RRR, relative risk reduction.

However, there is growing literature to suggest that apart from being the most prevalent group of fractures, NHNV fractures are also associated with significant adverse effects (4–7). A recent analysis of first-year direct health care costs of hip, vertebral, and NHNV fractures found that the proportion of total fracture costs due to NHNV fractures was 66% in the 50- to 64-year age group and 36% of total costs in those over 65 years (8). These high costs are related to the high percentage of NHNV fractures, particularly in the younger elderly.

It is also becoming more apparent that NHNV fractures contribute substantially to the burden of subsequent fractures (4, 9, 10). However, most of the studies have examined only a few specific fracture types, most commonly subsequent hip fracture after initial forearm fractures in women (11–13). Thus the overall contribution of NHNV fractures to subsequent fracture and particularly to subsequent hip and vertebral fracture has not previously been examined.

Premature mortality after fracture is well accepted for hip and vertebral fracture but more controversial for other fracture types (5, 6, 14–19). We have recently demonstrated an increased mortality after all fracture types (6). As expected, this increased mortality was highest after hip and vertebral fractures but still significantly increased for major and even for minor fractures in those over 75 years.

The aims of this study were two-fold: 1) to examine the total burden of subsequent fracture and premature mortality associated with NHNV fractures in elderly men and women using a competing risk model and 2) to compare these with subsequent fracture and premature mortality after initial hip and vertebral fracture.

The present study differs from previously presented data on refracture and mortality from this cohort in the following respects: increased length of follow-up, with more fracture outcomes collected; focus on the NHNV fracture group; and modeling of the data in a competing risk model that examines both subsequent fracture and mortality in a single model, overcoming the flaws inherent in Kaplan-Meier analysis when competing outcomes occur with high frequency.

Materials and Methods

Study population

The Dubbo Osteoporosis Epidemiology Study started in 1989 and is an ongoing study of community dwelling women and men aged 60+ residing in the city of Dubbo, approximately 400 km northwest of Sydney, Australia. The study has been approved by the St Vincent's Hospital human research ethics committee. A detailed description of the study has been previously published (20), but in summary, the city of Dubbo was chosen for its relative isolation, centralized health services, stable population, and similar age and sex distribution as the Australian population. The loss to follow-up was estimated at <6%. In 1989 the population was 32 000 of whom 98.6% were Caucasian. The population aged 60+ years consisted of 2245 women and 1760 men, of whom 952 women and 343 men sustained at least one minimal trauma fracture.

Fracture and mortality assessment

Fractures were identified from x-ray reports from the two and, for some time, three clinical radiological practices that service the entire Dubbo area. One practice is associated with the teaching hospital in Dubbo and the others, independent. Circumstances surrounding the fracture were obtained by personal interview using a scripted text and with a drop-down menu for data entry. High trauma and potentially pathological fractures (eg, from cancer or Paget's disease) as well as fractures of the fingers, toes, and skull were not included.

Fractures were classified as hip, vertebral, and NHNV. There was no systematic screening for vertebral fracture. Vertebral fractures were considered clinical if the x-ray was performed for a specific cause (eg, back pain) and incidental if no specific cause was identified. Clinical and incidental vertebral fractures had similar increased risk of subsequent fracture and mortality (data not shown [5]), so for this study, they were combined. NHNV fractures include all the remaining fractures except fractures of the head, fingers, and toes. The predominant fractures in this group were wrist (37% in women, 12% in men), ribs (10% in women, 36% in men), humerus (18% in women, 13% in men), and ankle (9% in women, 13% in men). Clavicle, sternum, distal femur, pelvis, tibia and fibula, metatarsal, and metacarpal fractures represented less than 7% each.

Mortality status of all fracture subjects was identified from systematic searches of funeral director lists, local media, and newspaper reports. These were verified in most cases by death certificates obtained from the New South Wales Registry of Births, Deaths, and Marriages. Population data for the whole Dubbo area were obtained from the Australian Bureau of Statistics for each year of the study for each age group.

Apart from the fracture data, detailed baseline characteristics were not collected on the participants in this study. However, there was a detailed study group comprising 61% of the fracture group that has previously been described (4, 6). They had a mean (±SD) age of 73 (7) years in both sexes, similar to the whole fracture population presented, body mass index of 25 (5) for women and 26 (4) for men; 29% of women and 62% of men smoked; 3% of women and 4% of men had a high alcohol intake, and 47% of women and 38% of men had no comorbidities. Refracture rates and standardized mortality ratios (SMR) were not statistically different between this group and the whole fracture group, although the women in the detailed study group tended to have a lower SMR and higher refracture rate, consistent with healthy study entrant bias.

Statistical analysis

Initial fracture rates were calculated as annual incidence based on the population data in 5-year age groups. Once a person had a fracture, he or she was excluded from the population at risk. For the refracture analyses, follow-up time was calculated from the first fracture until the second fracture, death, or end of

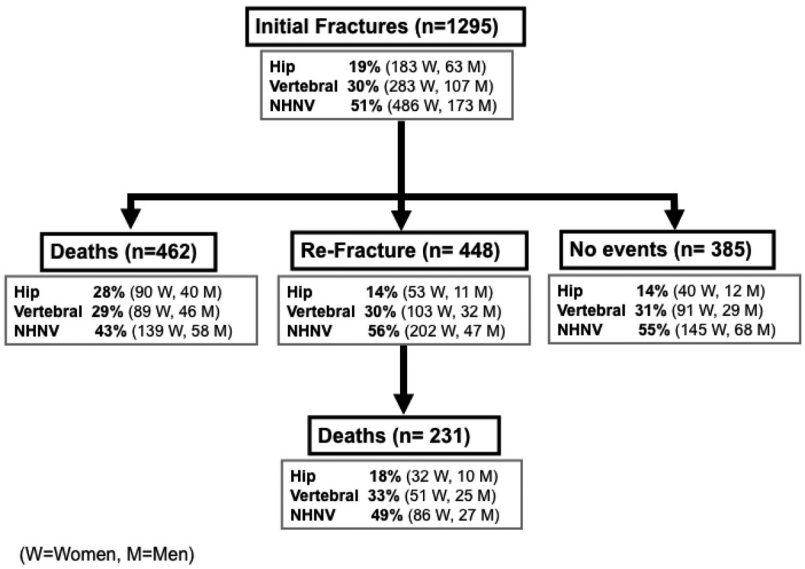

Figure 1. Flow chart of the participants in the Dubbo Osteoporosis Epidemiology Study.

the study (January 2011). Relative risk of refracture was based on the comparison of the refracture rate with initial fracture rates. Relative risks and confidence intervals (CI) were based on Poisson assumptions and were two-sided.

Age- and gender-specific life tables of expected survival in the general population were created based on data from the Australian Bureau of Statistics, to match the hip, vertebral, and NHNV fracture cohorts, calculated in 5-year age groups. The annual number of excess deaths was calculated using the SMR.

The total burden of postfracture adverse events of refracture and mortality was evaluated separately for hip, vertebral, and NHNV fractures using a single competing risk model with four possible outcomes: death after initial fracture, death after refracture, refracture and alive, or event-free (21).

The cumulative incidences of these postfracture events were plotted in a stacked graph, such that the distance between the curves represents the probability of different postfracture events (Figure 3).

All statistical analyses were performed using SAS version 9 (SAS Institute, Inc).

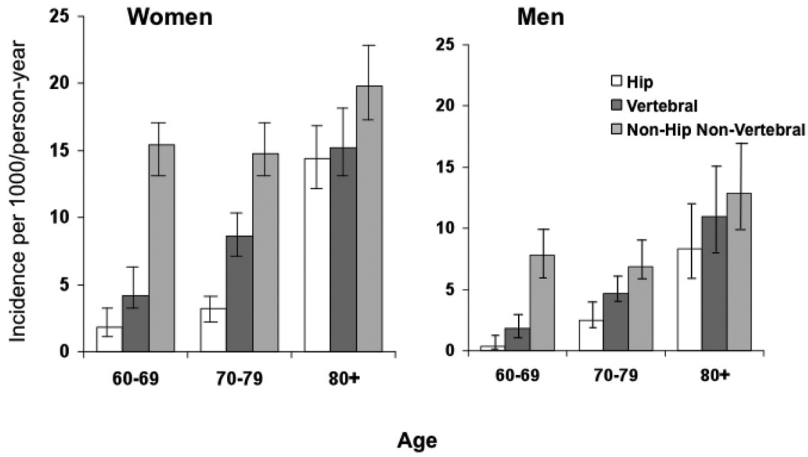

Figure 2. Cumulative incidence of initial fracture type in Dubbo population according to age women and men.

Results

Fracture incidence

There were 1295 initial fractures (952 in women [183 hip, 283 vertebral, and 486 NHNV] and 343 in men [63 hip, 107 vertebral, and 173 NHNV]) over 29 660 person-years in women and 20 717 person-years in men. During this period, another 448 subsequent fractures occurred (358 in women and 90 in men) over 5779 person-years in women and 1886 person-years in men. NHNV fractures accounted for over half of both initial and subsequent fractures (Figure 1).

Although initial fracture rates increased exponentially with age for hip and vertebral fractures in both women and men (Figure 2), NHNV fracture incidence remained more constant with increasing age. Thus, in the younger age groups, NHNV fractures dominated the fractures. For example, in the 60- to 69-year age group, NHNV fracture incidence was 15.4/1000 person-years (95% CI, CI 12.7–18.8) in women and 7.8/1000 person-years (95% CI, 5.8–10.4) in men, compared with hip fracture rates of 1.8/1000 person-years (95% CI, 1.0–3.2) in women and 0.4/1000 person-years (95% CI, 0.1–1.4) in men. However, even in the 80+ year age groups, the incidence of NHNV fractures was greater than that of hip or vertebral fractures alone.

Subsequent fracture risk

For all types of fractures, the absolute and relative risk of subsequent fracture was increased (Table 1). The risk of a subsequent fracture was higher after an initial hip and vertebral fracture than a NHNV fracture, although not significantly so. The higher relative risks of subsequent fracture after an initial hip/vertebral fracture were due to the very high risks in the younger age groups, particularly in men. Importantly, in the older age groups, the relative risks of subsequent fracture were comparable across all fracture types.

Subsequent hip fracture

Hip refracture was increased after all types of initial fracture, although the rate of subsequent hip fracture was higher after initial hip than after initial NHNV fracture (Table 2).

Table 1. Absolute and Relative Refracture Risk According to Initial Fracture Type

	Women				Men			
Initial Fracture Type	Person-Years	Refracture (n)	Rate per 1000 Person-Year (95% CI)	RR (95% CI)	Person-Years	Refracture (n)	Rate per 1000 Person-Year (95% CI)	RR (95% CI)
Hip								
All ages	751	53	71 (54–92)	2.39 (1.82–3.17)	217	11	51 (28–92)	3.25 (1.78–5.93)
60–74	138	11	80 (44–144)	3.59 (1.97–6.56)	102	4	39 (15–105)	4.01 (1.48–10.87)
75+	613	42	69 (51–93)	1.93 (1.41–2.64)	115	7	61 (29–127)	2.61 (1.23–5.55)
Vertebral								
All ages	1513	103	68 (56–83)	2.37 (1.93–2.90)	458	32	70 (49–99)	4.52 (3.14–6.49)
60–74	535	31	58 (41–82)	2.67 (1.85–3.87)	145	10	69 (37–128)	6.95 (3.64–13.25)
75+	979	72	74 (58–93)	2.12 (1.66–2.70)	312	22	70 (46–107)	3.10 (2.00–4.80)
NHNV								
All ages	3515	202	57 (50–66)	1.95 (1.67–2.27)	1211	47	39 (29–52)	2.47 1.82–3.35)
60–74	1990	85	43 (35–53)	1.97 (1.55–2.51)	744	24	32 (22–48)	3.33 (2.14–5.16)
75+	1525	117	77 (64–92)	2.14 (1.76–2.61)	468	23	49 (33–74)	2.13 (1.39–3.28)

Similarly, this was only observed in younger individuals (<75). In the older age group (75+), the incidence of hip refracture was similar after all initial fracture types.

Subsequent vertebral fracture

A subsequent vertebral fracture was as common as subsequent hip fracture. In women, the risk of a subsequent vertebral fracture was similar after either NHNV or hip and vertebral fractures and approximately two-fold higher than the risk of an initial vertebral fracture in the fracture-naive population. In men, an initial NHNV fracture was associated with a two-fold increased relative risk of subsequent vertebral fracture, although this risk was lower than that after initial hip or vertebral fracture (Table 2).

Competing risk of mortality and subsequent fracture

The pattern over time and the relationship between all possible postfracture outcomes (death after the initial fracture, death after subsequent fracture, subsequent fracture and alive, or event-free) were assessed using competing risk models with participants stratified by gender and initial fracture type.

Mortality after the first osteoporotic fracture

The mortality was highest in the first 5 years postfracture for all types of osteoporotic fractures as seen by the slope of the dotted line (Figure 3), which is steepest in the first few postfracture years before leveling off. Mortality was greater in men than women and was highest for hip, followed by vertebral and NHNV fractures. Compared with the mortality rates in the population, excess deaths were observed for all types of osteoporotic fractures. At 5 years, the excess deaths were 24% for women and 31% for men after hip fracture, 10% for women and 15% for men after vertebral fracture, and 8% for women and 9% for men after NHNV fracture (Table 3).

After the first 5 years, mortality decreased significantly, reaching population mortality, except for the hip fracture cohort, where 17%–20% of excess deaths were observed for up to 10 years postfracture.

Subsequent fracture risk after initial fracture

Of those who survived the first fracture, an additional 30%–40% of participants experienced a subsequent fracture. Similar to mortality risk after an initial fracture, subsequent fracture risk was higher in the first 5 years post-

Table 2. Hip and Vertebral Refracture Risk

	Hip Refracture		Vertebral Refracture	
Initial Fracture Type	Rate per 1000 Person-Year	RR (vs initial hip rate)	Rate per 1000 Person-Year (95% CI)	RR (vs initial vertebral rate)
Women				
Hip	25 (16–40)	4.05 (2.53–6.50)	20 (12–33)	2.10 (1.25–3.52)
Vertebral	17 (12–25)	2.76 (1.83–4.16)	21 (15–30)	2.20 (1.53–3.17)
NHNV	13 (9–17)	2.11 (1.04–4.28)	18 (14–23)	1.89 (1.43–2.48)
Men				
Hip	14 (5–43)	4.61 (1.45–14.66)	18 (7–49)	3.49 (1.29–9.46)
Vertebral	17 (9–35)	5.59 (2.68–11.67)	26 (15–46)	5.04 (2.77–9.15)
NHNV	8 (4–15)	2.63 (1.35–5.13)	11 (6–18)	2.13 (1.20–3.79)

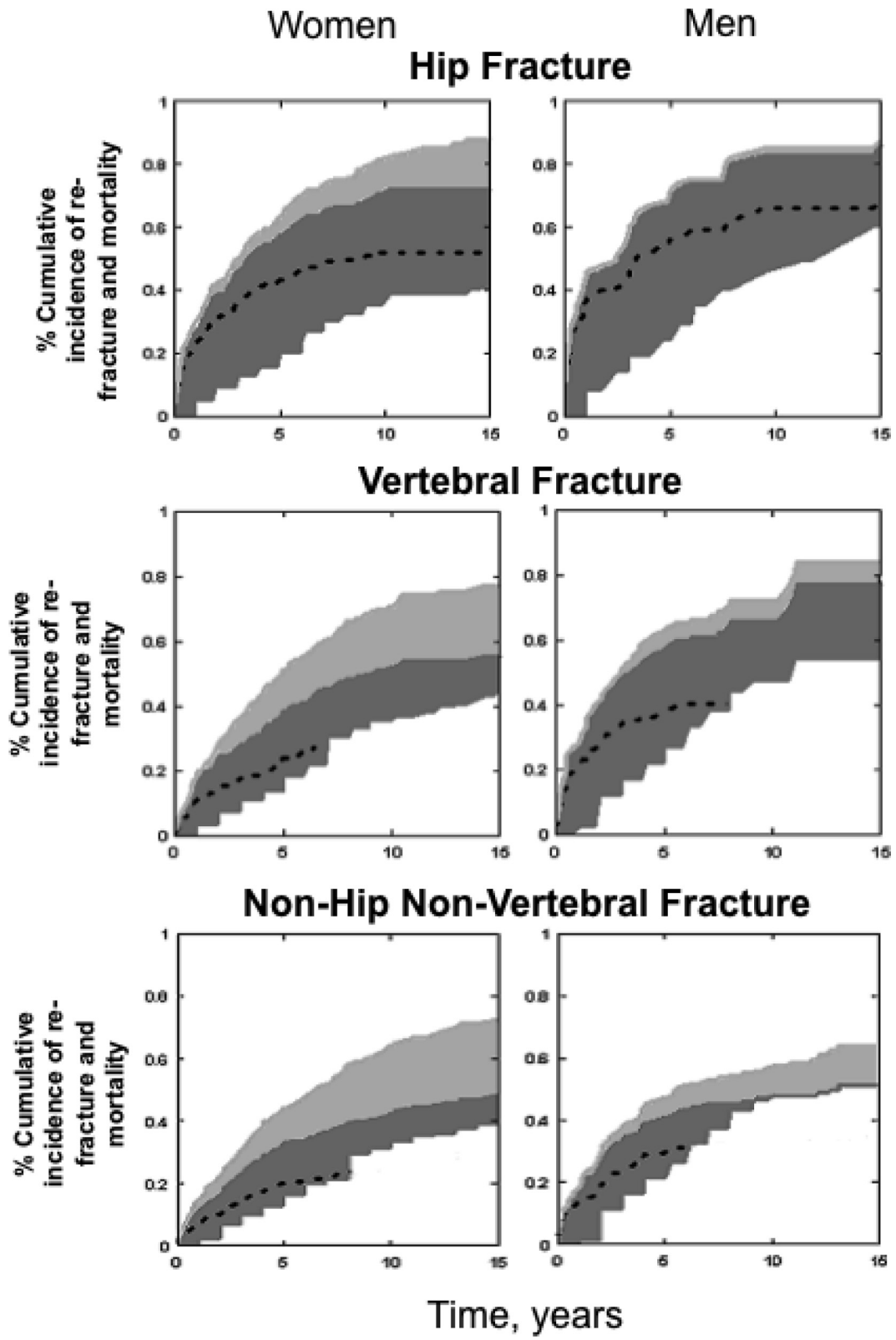

Figure 3. Stacked graph of cumulative incidences of refracture and mortality after one osteoporotic fracture and after refracture compared with an age-matched general population for hip, vertebral, and NHNV fracture in women (left) and men (right). This graph is composed of three main bands: The white band at the bottom of the graph represents the expected mortality in an age-matched general population. The dark gray band represents the excess deaths observed in the fracture population. A dotted line separates the dark gray band into a lower band representing the excess deaths after the initial fracture and an upper band representing the excess deaths after refracture. The light gray band represents those who had a refracture and were alive at the end of the study.

Table 3. Estimated Excess Mortality After Initial and Refracture According to Initial Fracture Type for the First 5 years Postfracture

Initial Fracture Type	Fracture Cohort		% Estimated Excess Deaths		
	First Fracture, N	Deaths, N (%)	Total	First Fracture	Refracture
Women					
Hip	183	118 (64)	38	24	14
Vertebral	283	133 (47)	21	6	15
NHNV	486	210 (43)	20	8	12
Men					
Hip	63	50 (79)	45	31	14
Vertebral	107	65 (61)	35	15	20
NHNV	173	82 (47)	20	9	11

These estimates were derived from the competing risk model of refracture and mortality and represent the difference between probability of deaths in the fracture cohort and that in the age-matched general population.

fracture for both women and men. Beyond this interval, there were very few subsequent fractures in men due to their high mortality rate. For women, although lower than immediately after the initial fracture, subsequent fracture risk was still elevated up to 15 years after the initial fracture, particularly for NHNV fractures.

Mortality risk after subsequent fracture

Notably, subsequent fracture was associated with significantly increased mortality risk, contributing to 11%–20% of excess deaths at 5 years (Table 3) and most of the excess mortality at 10 years. Men fared worse after a subsequent fracture than after the initial fracture, with mortality up to 80%–90% for those who suffered a subsequent fracture after a hip or vertebral fracture and over 50% for subsequent fracture after an initial NHNV fracture (Figure 3).

Age-adjusted SMR

Age-adjusted SMR were elevated for the first 5 years postfracture for all types of osteoporotic fracture. The highest mortality was observed for hip fracture (2.10 [95% CI, 1.70–2.60] for women and 2.95 [95% CI, 2.16–4.03] for men), followed by vertebral fracture (1.44 [95% CI, 1.17–1.77] for women and 1.94 [95% CI, 1.48–2.54] for men) and NHNV fracture (1.34 [95% CI, 1.12–1.61 for women] and 1.51 [95% CI, 1.17–1.95] for men).

To determine whether the observed increased mortality risk after NHNV fracture was mediated through a hip or vertebral subsequent fracture, a subset analysis of individuals with initial NHNV fracture, but who did not have a subsequent fracture, was performed. Mortality risk was still >60% higher in this group than in general population (2.00 [95% CI, 1.63–2.45] and 1.60 [95% CI, 1.20–2.14] in women and men, respectively).

The effect of fracture type on mortality risk after NHNV fractures

NHNV fractures were further classified into distal fractures, including wrist, metacarpal, ankle, and metatarsal fractures, and proximal fractures, including rib, humerus, proximal tibia/fibula, pelvis, and clavicle. Proximal fractures were associated with increased mortality risk in both women and men (age-adjusted SMR: 1.61 [95%CI, 1.28–2.04] for women and 1.67 [95% CI, 1.26–2.22] for men), whereas distal fractures were associated with increased mortality risk only in the group who sustained a subsequent fracture (age-adjusted SMR 1.49 [95% CI, 1.08–2.06] for women and 2.15 [95% CI, 1.22–3.79] for men).

Causes of death

Death certificates were analyzed for 72% of fractures. There were no differences in the major causes of death between NHNV fractures and either hip or vertebral fractures with the major causes of death being similar to that of the general population (cardiac 21%–31%, respiratory 22%–31%, cerebrovascular 14%–16%, and malignancy 10%–12%).

Population-attributable risk

With the high prevalence of NHNV fractures being 51% of all fractures, a large proportion of subsequent fractures followed these initial NHNV fractures. Thus the population-attributable risk of any subsequent fracture after an initial NHNV fracture was high, ranging from 29% in women to 41% in men. Similar results were obtained for a subsequent hip or vertebral fracture after an initial NHNV fracture (30% in women and 46% in men).

For a similar reason, the population-attributable risk of the excess mortality associated with fracture was similar between all initial fracture types, approximately 18% in

women and 25% in men, again relating to the high prevalence of NHNV fractures.

Discussion

In this 20-year community-based prospective study, NHNV fractures not only represented half of all initial low trauma fractures, but also preceded approximately half of all subsequent fractures and a quarter of excess mortality related to fracture. Subsequent fracture risk was similarly increased after both NHNV and hip/vertebral fractures. Most importantly, mortality risk was increased for the first 5 years postfracture for NHNV fractures as well as hip and vertebral fractures. Subsequent fracture contributed substantially to the overall mortality risk, but notably, the increased mortality risk observed after NHNV fracture persisted even when the analysis was restricted to those who did not experience any subsequent fracture except for the subgroup of peripheral fractures.

This study demonstrated a high cumulative incidence of subsequent fracture and mortality after NHNV as well as hip and vertebral fractures. In the first 5 years after a NHNV fracture, approximately 20%–30% of individuals died after the initial fracture, and 17%–24% had suffered a subsequent fracture, with a further 9%–12% dying after the second fracture, bringing the total mortality to 29%–42%. Although this risk of subsequent fracture and premature mortality was approximately 10%–20% lower than for vertebral and hip fractures, respectively, the higher prevalence of NHNV fractures meant that the total number of subsequent fractures and deaths in the overall population was similar for hip, vertebral, and NHNV fractures. Thus population-attributable risk for both subsequent fracture and mortality was similar for all types of initial fracture.

Subsequent fracture risk after all osteoporotic fractures is well described (9, 22). The role of prior fracture type on the risk of subsequent fracture has been explored mainly for individual types of fracture, such as hip, vertebral, forearm fracture, with most data being reported in women rather than men. This study confirmed the high risk of subsequent fracture for the NHNV fracture group. NHNV fractures were associated with approximately two- to three-fold risk of a subsequent fracture, including hip and vertebral subsequent fracture. This risk was slightly lower than that observed for hip and vertebral fractures in those <75 years. However, for those >75 years of age, subsequent fracture risk was similar for all fracture types.

The high rate of subsequent fracture including hip and vertebral fractures after an initial NHNV fracture is highly relevant when considering treatment intervention and effectiveness. It is well documented that <30% of women and <10% of men receive appropriate antiresorptive therapy after initial fracture. Nevertheless, the data on secondary prevention are more compelling than for primary prevention, particularly for nonvertebral fractures. In a recent Cochrane review of Alendronate, although reduction of vertebral fracture was significant for both primary and secondary prevention (45% relative risk reduction, RRR), reduction of both hip and NHNV fractures was only significant for secondary prevention where there was a 23% RRR of nonvertebral fractures and 53% RRR of hip fractures (23). Thus, NHNV fractures, even the more peripheral ones, should be targeted for treatment intervention, given the high subsequent hip or vertebral fracture.

Importantly, NHNV fractures were associated with increased mortality risk in a stratified unadjusted analysis. Approximately half of the mortality observed in the first 5 years after NHNV fractures were above that expected for an age- and gender-matched general population, resulting in a total excess mortality of 20% in both women and men in the first 5 years after initial fracture. More than half of this excess mortality were related to a subsequent fracture. Notably, this excess mortality was not driven entirely by an elevated risk of a more major subsequent fracture, such as hip or vertebral fracture. Even when the analysis was restricted to those who had had just one NHNV fracture, there was 9% excess mortality. However, for the distal minor fractures (such as ankle, foot, wrist, and hand), all excess mortality was associated with a subsequent fracture.

Premature mortality associated with osteoporotic fracture has been previously reported and is accepted for hip and vertebral fractures, but very few studies have addressed mortality risk after NHNV fractures. Recently, Huntjens et al (14) reported increased mortality risk associated with nonvertebral fractures, while others have reported increased mortality risk associated with humerus fractures (18, 19). There is a generally accepted opinion that minor or peripheral fractures, such as wrist or forearm fractures, are not associated with increased mortality risk (19, 24). However, we previously demonstrated an excess mortality associated with minor fractures when the analysis was restricted to older people (6). The present study has demonstrated that the excess mortality associated with minor fractures was due to subsequent fractures that may not have been accounted for in the earlier studies. However, the more proximal NHNV fractures were associated with increased mortality even without a subsequent fracture, which may relate to their greater disability for an elderly person.

This study was consistent with previous findings of a higher mortality in men than women. This discrepancy was most apparent after a subsequent fracture, particularly after an initial hip or vertebral fracture. The cause for the increased mortality in men is not clear, although one previous study of hip fractures did not find it to be related to comorbidities (25).

It is important to acknowledge that this study cannot determine the cause of the increased premature mortality observed after fracture. We have previously examined death certificates for the fracture cohort and found the causes to be similar to that of the general population with most deaths related to cardiovascular, respiratory, and neurological causes. There were no differences between causes of death after NHNV fractures or after hip or vertebral fracture. It is unlikely that the NHNV fracture per se directly leads to premature death. However, in an elderly, frail person it is possible that the fracture represents an event that results in a downward spiral of health and social changes that contribute to premature mortality.

This study has several strengths. It examined a large population-based cohort over 20 years. This was essential for the examination of all possible postfracture outcomes, including mortality after subsequent fracture. The relatively large and stable cohort, made possible the evaluation and comparison of both age- and gender-specific adverse events with very low loss to follow-up. Furthermore, any loss to follow-up would only have resulted in an underestimation of subsequent mortality or refracture. There are some limitations. First, the study population is almost entirely Caucasian; thus, these findings cannot be directly extrapolated to other populations or ethnic groups. Second, the fracture types included in the NHNV fracture group were heterogeneous with some fracture types having a higher subsequent fracture or mortality risk than others. Third, given the long follow-up and the high mortality after fracture, there were few people left alive after 10 years of follow-up. However, this was predominantly for the older rather than the younger NHNV fracture group. Finally, this study cannot prove causality between fracture and premature mortality but only demonstrates an association between them. Population-attributable risk is a mathematical formula, dependent on the frequency of the presumed risk factor, in this case fracture, and does not mean that fracture was the direct cause of death but associated with it (26).

In summary, NHNV fractures represented half of all osteoporotic fractures occurring in the community, with the burden of these fractures occurring in younger individuals. All osteoporotic fractures, and not only hip and vertebral, were associated with a high incidence of subsequent fracture and premature mortality. Both subsequent fracture and mortality were higher in the first 5 years after initial fracture; however, subsequent fracture risk persisted beyond this interval, particularly in those with NHNV fractures and in women. Notably, NHNV fractures were associated with 20%–30% excess deaths in the first 5 years after fracture, with half of this excess occurring in those who had only one fracture. However, for the distal minor fractures, all excess mortality was only associated with a subsequent fracture. Finally, based on their high prevalence, NHNV fractures contributed to half of all the subsequent fractures and deaths attributable to a fracture event.

Much research and clinical intervention have been focused on hip and vertebral fractures, with NHNV fractures receiving far less attention. However, this study clearly demonstrates that NHNV fractures are associated with both significant risk of subsequent fracture, including that of the hip and spine, as well as premature mortality. Thus early intervention after NHNV fractures to reduce the high risk of subsequent fracture and their adverse outcomes should be recommended.

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