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Mortality after all major types of osteoporotic fracture in men and women: an observational study

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Summary

Background Mortality increases after hip fractures in women and more so in men. Little is known, however, about mortality after other fractures. We investigated the mortality associated with all fracture types in elderly women and men.

Methods We did a 5-year prospective cohort study in the semi-urban city of Dubbo, Australia, of all residents aged 60 years and older (2413 women and 1898 men). Low-trauma osteoporotic fractures that occurred between 1989 and 1994, confirmed by radiography and personal interview, were classified as proximal femur, vertebral, and groupings of other major and minor fractures. We calculated standardised mortality rates from death certificates for people with fractures compared with the Dubbo population.

Findings 356 women and 137 men had low-trauma fractures. In women and men, mortality was increased in the first year after all major fractures. In women, age-standardised mortality ratios were 2·18 (95% CI 2·03–2·32) for proximal femur, 1·66 (1·51–1·80) for vertebral, 1·92 (1·70–2·14) for other major, and 0·75 (0·66–0·84) for minor fractures. In men, these ratios were 3·17 (2·90–3·44) for proximal femur, 2·38 (2·17–2·59) for vertebral, 2·22 (1·91–2·52) for other major, and 1·45 (1·25–1·65) for minor fractures. There were excess deaths (excluding minor fractures in women) in all age-groups.

Interpretation All major fractures were associated with increased mortality, especially in men. The loss of potential years of life in the younger age-group shows that preventative strategies for fracture should not focus on older patients at the expense of younger women and of men.

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Introduction

Although osteoporosis and related fractures are well-recognised public-health concerns, their impact on mortality remains unclear. Increased mortality after hip fracture is generally accepted, but there are few data on the outcomes of other fracture types. Excess mortality varies after hip fracture, with 12-month rates ranging from 12% to 35%.[1] The variation in these mortality estimates may relate to differences in demography, age of people studied, study size, and completeness and length of follow-up. Most excess mortality occurs within the first 3–12 months after fracture,[2–5] and increases with age.[5–11]

In women, low bone-mineral density has been associated with increased mortality independent of fracture.[12,13] At least some of the fracture-mortality association may, therefore, reflect the underlying health of the individual. Although comorbid health status has been associated with mortality after hip fracture in most studies,[3,5–7,14–19] this finding has not been universal.[20]

If osteoporosis is independently associated with mortality, increased mortality could be associated with other types of osteoporotic fractures. In one population-based study, women with vertebral fractures had increased 5-year mortality.[21] These were clinically diagnosed vertebral fractures that may represent only a third of all vertebral deformities. By contrast, the survival of women with forearm fractures,[21–23] foot, or ankle fractures[23] has been reported to be no different from that of the general community.

In men, several studies have investigated mortality after hip fracture but not other fracture types. Direct comparisons of results when possible have shown that survival seems to be worse in men than in women.[3–7,9,10,17,24]

We investigated mortality associated with all osteoporotic fractures in an elderly community cohort.

Methods

Patients

Dubbo is a semi-urban city 400 km northwest of Sydney, Australia. The population is about 32 000, of which 98·6% of people are white. The community is stable with its own centralised health services, and is representative of the Australian population.[25]

The Dubbo Osteoporosis Epidemiology Study is a longitudinal epidemiological study assessing risk factors for osteoporosis and fractures, which started in July, 1989. As part of that study, all radiography reports from the whole Dubbo population aged 60 years and older are reviewed and fractures identified. Two radiology centres serve the area, which enables us to obtain details of almost all fracture events coming to clinical attention.

For our study, the population consisted of 2413 women and 1898 men resident in the Dubbo area between July, 1989, and November, 1994, which represents the entire population aged 60 years and older. Apart from age, there were no specific entry criteria.

Methods

The fractures that were identified had the circumstances surrounding the fracture recorded by personal interview. We included only low-trauma fractures caused by falls from standing height or less. Vertebral fractures identified were those coming to clinical attention. No systematic radiographic screening was done before the study to identify prevalent fractures. To try to differentiate incident from prevalent vertebral fractures during the study, we classified fractures as incident if the clinical history suggested recent symptomatic fractures or previous radiographs showed no evidence of fracture. Prevalent fractures included all vertebral fractures identified. We excluded any person with an underlying disorder, such as cancer or bone disease, that could cause pathological fracture.

We analysed fractures by the following classifications: proximal femur, vertebral, other major, and minor. Other major fractures excluded hip or vertebral fracture, but included pelvic, distal femur, proximal tibia, multiple rib, and proximal humerus. Minor fractures included all remaining osteoporotic fractures, including distal arm and leg. We analysed all vertebral fractures combined, as well as separated into incident and prevalent status.

Mortality status for the fracture patients was assessed during 5-year follow-up, ending November, 1994, by searches of official death certificates from the New South Wales Registry of Births, Deaths, and Marriages, matched for name, age, and address. These records were cross-referenced with local Dubbo records to verify accuracy. If the identity of any patient on the death certificate was in question, we made all possible attempts to contact the patient at the last known address. In only one case was the patient's identity not confirmed, and this death was not included in the study.

Statistical analysis

For the entire Dubbo population, we calculated age-specific and sex-specific Dubbo mortality rates based on the actual number of deaths and mid-year population obtained from the Australian Bureau of Statistics.[26] For all patients who had osteoporotic fractures, we calculated observed age-specific and sex-specific mortality rates for each type of fracture, with the length of follow-up (person-years), based on the time between the fracture event and death or the end of the study. Expected number of deaths for each type of fracture, based on sex and age at time of fracture, was calculated from the Dubbo mortality rates. We then calculated standardised mortality ratios for observed to expected

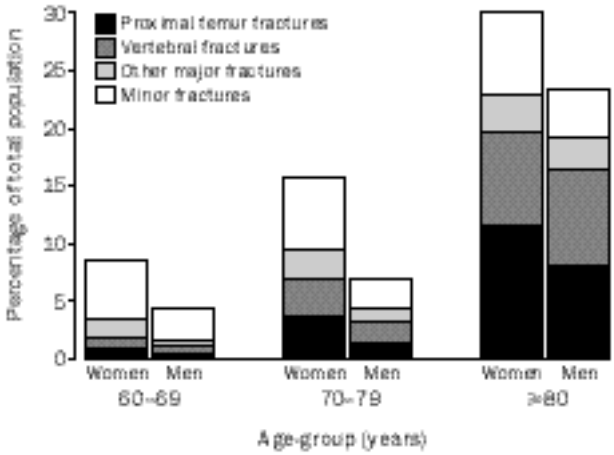

Figure 1: **Percentage of Dubbo population with fractures by sex and age-group**

deaths for each fracture type. Significance and 95% CIs for standardised mortality ratios were based on the Poisson assumption and are two-sided.[27] Excess mortality was calculated in 10-year age-groups by subtraction of the expected deaths in the Dubbo population (Australian Bureau of Statistics data) from the observed deaths among fracture patients. These data were extrapolated to the Australian and the US general populations according to 1994 mid-year population figures (Australian Bureau of Statistics and US Bureau of the Census).

Age-specific and sex-specific life tables were constructed separately for the entire Dubbo population and fracture patients. We plotted cumulative survival probabilities from these tables. For fracture patients, follow-up in person-years was based on the time from fracture until death or study end. Calculations were based on the 5-year age-group in which the fracture occurred. We compared differences in survival probabilities between fracture patients and the Dubbo population by log-rank statistic.[28] Life-expectancy was estimated by life-table analysis. We calculated years of life lost as the difference between the life expectancy for the entire Dubbo population and that of the fracture group in particular 10-year age-groups.

To quantify the risk of mortality due to fractures, attributable risk was calculated as:

$$p(RR-1)/[p(RR-1)+1],$$

where p is the proportion of patients in the sample who had a fracture and RR is the relative risk of fracture for fracture

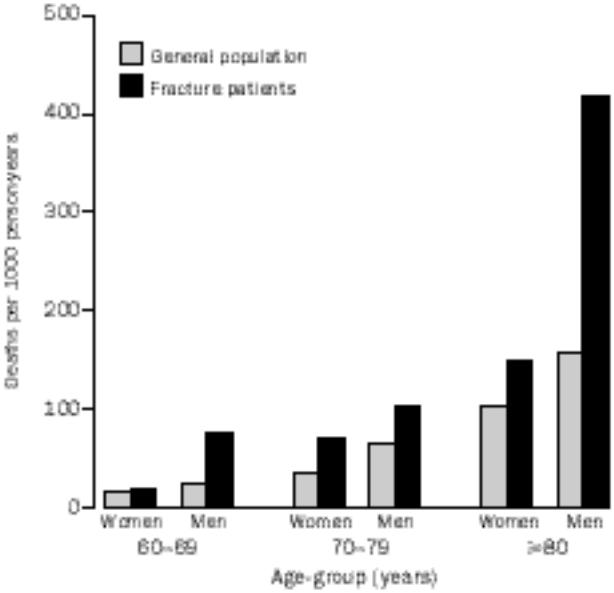

Figure 2: **Mortality rates for fracture patients and general population by sex and age-group**

Fracture type	Standardised mortality ratio (95% CI)
Women	
Proximal femur	2·18 (2·03–2·32)
Vertebral	1·66 (1·51–1·80)
Other major	1·92 (1·70–2·14)
Minor	0·75 (0·66–0·84)
Men	
Proximal femur	3·17 (2·90–3·44)
Vertebral	2·38 (2·17–2·59)
Other major	2·22 (1·91–2·52)
Minor	1·45 (1·25–1·65)

Table 1: **Standardised mortality ratio by sex and fracture type**

patients, estimated from the proportional-hazards model. In this formula, attributable risk is the proportion by which the incidence of mortality in the general population would be decreased if the risk of fractures (measured by p) were eliminated.[29]

Results

Between 1989 and 1994, there were 356 low-trauma fractures in women and 137 in men during 12 056 person-years and 9483 person-years of observation, respectively. The overall fracture incidence (per 1000 person-years) was 29·5 for women and 14·4 for men. In the two sexes, fracture rates increased with age, with an exponential increase for proximal femur and vertebral fractures. The increase for other major fractures was gradual, whereas incidence of minor fractures was generally constant. Among patients aged 80 years and older, 30% of women and 24% of men had fractures during the 5 years of observation (figure 1).

In the general population, there were 449 deaths among women and 472 deaths among men, equivalent to mortality rates of 37·2 and 49·7 per 1000 person-years, respectively. The mortality rates in fracture patients were 73·0 (58 deaths from 794 person-years of observation) in women and 166·5 (47 deaths from 282 person-years of observation) in men per thousand person-years. There were more deaths among fracture patients for each age-group than in the general population and more deaths per age-group in men than women (figure 2).

The fracture patients were significantly older than the general population (mean 75 [SD 8·7] *vs* 71 [8·9] years, p<0·001), and, therefore, age-standardised mortality ratios were calculated. Standardised mortality ratios were higher for men than women for all fracture types (table 1). Standardised mortality ratios were higher for incident and prevalent clinically diagnosed vertebral fractures. In women, the ratios were 1·6 (1·4–1·8) for incident and 1·8 (1·6–2·1) for prevalent vertebral fractures. In men, these ratios were 1·8 (1·6–2·0) and 3·7 (3·4–3·9). Standardised mortality ratios for all incident and prevalent vertebral

	Number of fractures	Number of deaths	Number of deaths by year after fracture (incidence/1000 person-years)		
			<1 year	1–2 years	2–5 years
Women					
Total number	345	58	36	4	18
Hip	76	24	15 (266·5)	2 (37·9)	7 (17·8)
Vertebral	76	16	9 (135·8)	1 (15·7)	6 (11·1)
Other major	53	9	8 (186·4)	0	1 (2·7)
Minor	140	9	4 (32·9)	1 (8·0)	4 (3·9)
Men					
Total number	137	47	33	5	9
Hip	27	15	10 (525·2)	1 (115·5)	4 (33·0)
Vertebral	38	17	12 (422·2)	2 (47·5)	3 (13·6)
Other major	17	6	5 (393·1)	0	1 (7·8)
Minor	55	9	6 (128·6)	2 (44·8)	1 (2·9)

Table 2: **Mortality and time to death by sex and fracture type**

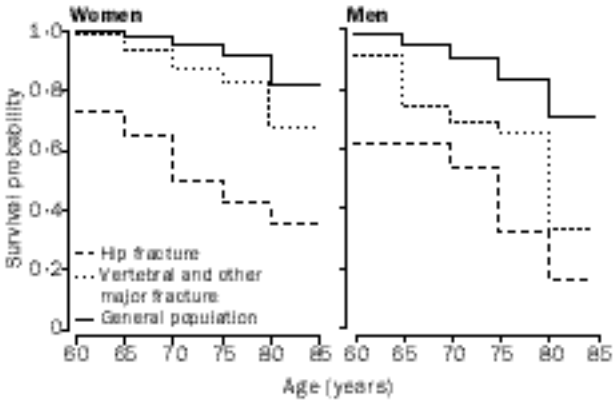

Figure 3: **Cumulative survival probability by sex and type of fracture**

fractures combined were also higher for men than women (table 1). The number of deaths by year after fracture is shown in table 2.

The cumulative probability of survival was estimated for the general population and fracture patients by fracture site (figure 3). For women and men, hip fracture was associated with significantly shorter survival than in the general population (both p<0·0001). In men and women, other non-hip major and vertebral fractures were also associated with significantly shorter survival (p=0·003 for women, p<0·0001 for men).

The average life expectancy for Dubbo women and men aged older than 60 years was estimated to be 24 years and 19 years, respectively. For fracture patients the expected remaining life years for those who fractured in the younger age-groups were decreased more than for those in the older age-groups (table 3).

Although death rates were higher in the older age-groups compared with younger age-groups for fracture patients and the general population, the larger numbers of patients in the younger age-groups meant that the excess death attributable to fracture was higher (table 4). Excess deaths were associated with all types of major osteoporotic fracture (figure 4). Among women aged 60–69 years, the observed excess deaths associated with proximal femur, vertebral, and other major fractures extrapolate to an excess of 261 deaths per year in Australia, equivalent to 3993 deaths in a directly age-standardised elderly population, comparable to that of the USA. In the same age-group of men, the corresponding excess deaths for proximal femur, vertebral, other major, and minor fractures were 5·5 in Dubbo, 689 in Australia, and 9303 for a USA directly standardised population.

Age-group	Life expectancy (potential years of life lost)		
	Dubbo population	Vertebral/other major fractures	Hip fractures
Women			
60–64	24·0	22·1 (−1·9)	12·8 (−11·2)
65–69	19·7	18·0 (−1·7)	13·7 (−6·0)
70–74	15·7	14·5 (−1·2)	11·3 (−4·4)
75–79	12·0	11·5 (−0·5)	10·8 (−1·2)
≥80	8·8	8·4 (−0·4)	8·4 (−0·4)
Men			
60–69	19·4	13·3 (−6·1)	7·9 (−11·5)
70–74	12·3	11·3 (−1·0)	6·9 (−5·4)
75–79	9·4	8·3 (−1·1)	4·8 (−4·8)
≥80	7·0	5·6 (−1·4)	5·5 (−1·5)

For men, 60–69-year age-group was not subdivided into 5-year ages because of smaller number of fractures, especially hip fractures.

Table 3: **Life expectancy in years for fracture and general population**

Age-group	Proportion of total population (%)	Relative risk	Attributable risk (%)
Women			
60–69	49·4	1·56	21·7
70–79	34·6	2·02	26·1
≥80	16·0	1·44	6·6
Men			
60–69	57·6	3·16	55·4
70–79	32·8	1·57	15·7
≥80	9·6	2·66	13·8

Table 4: **Attributable risk of mortality from fractures by age-group**

For all fracture patients, 9·5% of deaths were listed as directly due to fracture, almost all of which were of the hip. The other causes of death for the fracture patients included causes secondary to cancer (21·9%), cardiac disease (33·3%), and stroke (18·1%), similar to the Australian population. Since cancer deaths could have been associated with pathological fractures, despite efforts to exclude any fracture patients who had cancer, the standardised mortality ratios were recalculated, excluding all cancer deaths in the fracture group. For hip, vertebral, and all other major fractures, the standardised mortality ratio compared with the general population remained higher in men and women. In men with minor fractures, exclusion of cancer deaths decreased the ratio to values similar to that seen in women (0·7 [95% CI 0·5–0·8]).

Discussion

In an elderly population, we found that fracture patients had a higher mortality than did the general population, especially those with hip fractures. Men in all major fracture groups had consistently higher standardised mortality ratios (2·2–3·2) than women (1·7–2·2).

The attributable risk of mortality was higher in the 60–69-year age-group than in the 80-years-or-older age-group because of larger numbers. It was, therefore, not surprising to find a large number of excess deaths and strikingly decreased survival in the younger age-group, despite lower absolute death rates.

The estimated standardised mortality ratio (or magnitude of association) for women with hip fractures in our study is consistent with previous reports, including those from several large community-based studies.[5,20,23] The stronger association in men than women between hip fractures and mortality that we found has been shown previously.[3–7,9,10,17,24]

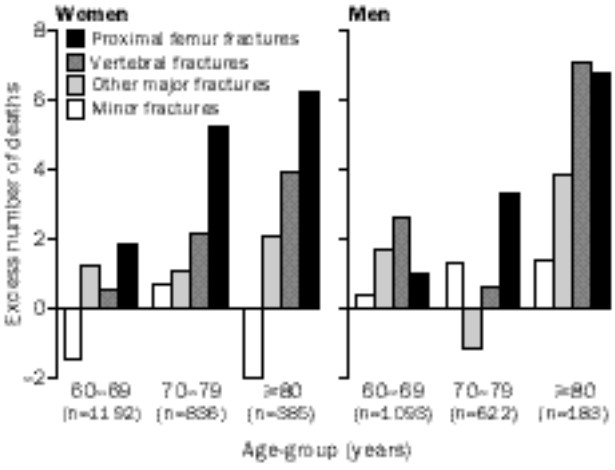

Figure 4: **Excess deaths over 5 years in Dubbo population by sex and age-group**

The association between mortality and fractures at other sites has been less well documented. The decreased survival probability for women with clinically diagnosed vertebral fractures was similar to the only published population-based study of mortality and vertebral fractures in women.[21] The increased mortality associated with vertebral fractures in men, which has not been documented previously, was comparable with that for men with hip fractures, and greater than that seen in women. The vertebral fractures that we included were, however, only those coming to clinical attention. Since routine radiography was not performed at study onset, symptomless, prevalent, or incident vertebral fractures, which may represent up to two-thirds of all morphometric vertebral deformities, may have been undetected. The separation of vertebral fractures into incident and prevalent classifications, may have misclassified those patients with no previous radiographs. There was, however, a consistent increase in mortality for men and women in the two groups of vertebral fractures, which, suggests that in clinically diagnosed vertebral fractures this increase in mortality is a real phenomenon.

We also found an association between increased mortality and a collective group of other major fractures, including pelvis, distal femur, proximal tibia, multiple rib, and proximal humerus in women and men. This association between all major fractures and increased mortality is consistent with the hypothesis that poorer underlying health in fracture patients contributes to increased mortality rather than just the fracture itself.[21] Browner and colleagues,[23] found that age-adjusted mortality rates in women for pelvic (in combination with hip), rib, and humeral fractures were higher than those for the non-fracture population. In that study, 53% of rib fractures were associated with underlying fatal disease. In our study there may have been a similar detection bias (sicker women more likely to seek medical attention) for vertebral and rib fractures, but it was kept to a minimum by exclusion of individuals with known underlying malignant disorders or bone diseases. Even with reanalysis excluding all cancer deaths in fracture patients there was still a higher mortality associated with hip, other major, and vertebral fractures in men and women.

Women with minor or distal fractures had a lower mortality than the general population. This finding is consistent with previous studies in which mortality after distal forearm fractures was the same as[21–23] or less than[30] that in the general population. This observation may also reflect the effect of underlying health on survival and even fracture, since women with wrist fractures have been found to be more healthy and active than the general population.[31] Men with minor fractures had a higher mortality than the general population, although the difference was less than that for major fractures. A plausible explanation for this finding, as well as the overall higher mortality in men than women, is that osteoporotic fractures, which are less common in men than women, are a reflection of poor underlying health in those men who do sustain them.

The underlying health hypothesis is supported by findings by others that, despite the sharp increase in mortality associated with hip fracture in older ages, the age-matched risk of dying was higher in the younger age-groups.[3,6] In our study, there were many excess deaths and significant decreases in survival for hip and other major fractures in the younger age-groups, especially in men.

The finding that most deaths occurred within 1 year of fracture may suggest an interaction between underlying health and fracture.

Our study had some obvious strengths. We investigated a stable population, which enabled assessment of almost all fractures and deaths. The large sample size and prospective design allowed assessment of finer differences that may not be detected in case-control studies. Our findings should, however, be interpreted within the context of several limitations. The population was mainly white; therefore, these results should not be extrapolated to other populations. The "other major fracture" group was heterogeneous and different mortality rates among individual major fractures types have been recorded previously.[23] There may have been selection bias for patients with vertebral fractures, which may have contributed to the higher mortality rate for prevalent than for incident vertebral fractures in men. This issue can be addressed only in studies of radiologically and clinically diagnosed vertebral fractures with sequential radiography done in an unselected population. The small numbers of fractures and deaths may have led to underestimation or overestimation of the exact excess deaths and years of life lost in specific age-groups. The overall pattern of increased mortality was, however, our major focus. Information on comorbid health status for all fracture patients was not available and, therefore, we could not find out whether the fracture event contributed to the mortality, or whether comorbidity contributed to the fracture and mortality. Irrespective of this relation, however, major fractures clearly identify a group at two-fold increased risk of mortality.

We have shown that increased mortality is associated with all major osteoporotic fractures in women and men. Although fracture and mortality rates were lower among people aged 60–69 years, this age-group constitutes a large proportion of the elderly population and contribute substantially to the number of excess deaths and shorter survival. The relative contribution of fracture compared with that from underlying health of the individual to mortality has yet to be determined, but osteoporosis-associated mortality has clearly been underestimated in women aged 60–69 years, and largely ignored in elderly men.

Contributors

Jacqueline Center designed the mortality study, obtained and analysed data, and drafted the manuscript. Tuan Nguyen advised and took an active role in the study design, analysis of data, and writing of the manuscript. Diana Schneider was involved in the initial data analysis and contributed to the final version of the manuscript. Philip Sambrook has had an active role in the conduct of the Dubbo Osteoporosis Epidemiological Study and contributed to the final version of the manuscript. John Eisman established the Dubbo Osteoporosis Epidemiological Study, and was involved in the conceptual discussions, analyses, and the various versions of the manuscript.

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