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Mortality following the first hip fracture in Norwegian women and men (1999–2008). A NOREPOS study ☆

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ABSTRACT

Hip fractures are associated with increased mortality and their incidence in Norway is one of the highest worldwide. The aim of this nationwide study was to examine short- and long-term mortality after hip fractures, burden of disease (attributable fraction and potential years of life lost), and time trends in mortality compared to the total Norwegian population. Information on incident hip fractures between 1999 and 2008 in all persons aged 50 years and older was collected from Norwegian hospitals. Death and emigration dates of the hip fracture patients were obtained through 31 December 2010. Standardized mortality ratios (SMRs) were calculated and Poisson regression analyses were used for the estimation of time trends in SMRs. Among the 81,867 patients with a first hip fracture, the 1-year excess mortality was 4.6-fold higher in men, and 2.8-fold higher in women compared to the general population. Although the highest excess mortality was observed during the first two weeks post fracture, the excess risk persisted for twelve years. Mortality rates post hip fracture were higher in men compared to women in all age groups studied. In both genders aged 50 years and older, approximately 5% of the total mortality in the population was related to hip fractures. The largest proportion of the potential life-years lost was in the relatively young-old, i.e. less than 80 years. In men, the 1-year absolute mortality rates post hip fracture declined significantly between 1999 and 2008, by contrast, the mortality in women increased significantly relatively to the population mortality.

Introduction

Osteoporotic fractures constitute a major health burden [1]. Hip fractures are the most serious osteoporotic fractures, mostly occurring late in life and associated with excess mortality [2,3]. Excess mortality associated with hip fracture is higher in men than in women regardless of age [3,4]. Patients with hip fracture may have a 5- to almost 8-fold increased risk of all-cause mortality during the first 3 months after the fracture [3]. This excess mortality seems to decline during the first two years post fracture, but does not return to the levels of the general population even 10 years after the fracture [3]. The relative contribution of the excess mortality post hip fracture to total population mortality has not been explored in depth, despite the considerable impact of osteoporosis-attributable hip fractures on mortality and societal health costs [5].

With improvement in medical care and life expectancy, a decline in mortality among hip fracture patients is to be expected. However,

☆ NOREPOS (The NORwegian EPidemiologic Osteoporosis Studies) is a collaboration between epidemiologic osteoporosis studies, which are sub-studies within large population-based surveys in four regions of Norway (Tromsø, Nord-Trøndelag, Hordaland, Oslo). The NOREPOS Hip Fracture Database includes all hospitalizations for hip fracture in Norway during 1994–2008.

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various studies indicate that absolute mortality within the first year after fracture remained unchanged between 1960 and 2000 [6–8]. A study of mortality in Norwegian hip fracture patients in Oslo, Norway, between 1978/79 and 1996/97 reported a decline in excess mortality over the first 6 months post fracture in male and female patients older than, but not younger than 85 years [9]. In Texas, hip fracture mortality decreased significantly in men, but not in women [10], whereas another US study concluded that hip fracture-related mortality declined between 1986 and 2005 in both genders [11]. On the other hand, a Danish study showed an increase in excess mortality among hip fracture patients between 1981 and 2001 [12]. In summary, both magnitude of and time trends in absolute and relative mortality following hip fracture differ between studies.

Norway has one of the highest rates of hip fracture in the world. The aim of the present study was to examine mortality after hip fracture in all patients in one country focusing on: a) excess mortality up to 12 years after the fracture in relation to gender and age, b) potential life years lost and the attributable risk of hip fracture on total mortality in the population, and c) impact of clinical care and treatment by assessing trends in absolute and relative mortality after hip fracture by year of fracture.

Methods

Identification of hip fractures and deaths

Data on hip fractures treated in Norwegian hospitals (1994–2008) were retrieved as previously reported [13]. About 75% re-fractures occur within five years after a first hip fracture [14]. For the present analysis, only first hip fractures occurring after 1998 were included to minimize classifying a second hip fracture as the first. Hence, all subjects sustaining a fracture before 1999 were excluded. A detailed description of the quality assurance, classification and validation of the NOREPOS Hip Fracture Database (NORHip) is available as supplemental material to a published paper [13]. In short, Patient Administration Systems from all 48 hospitals/health trusts in Norway treating hip fracture patients provided information on discharge diagnoses, surgical procedure codes and any additional diagnosis codes. Hospital stays were classified as incident or not incident based on diagnosis codes: International Classification of Diseases, Tenth Revision (ICD-10): S72.0–S72.2. The unique 11-digit personal identification number assigned to each Norwegian resident was used to identify hospitalizations for hip fracture and identification of first and second hip fractures in the period. Age at discharge was calculated. Persons 50 years or older who fractured between 1 January 1999 and 31 December 2008 were included in analyses. Death and emigration dates of the hip fracture patients were obtained from the National Population Register from 1st of January 1999 to 31st of December 2010.

Population data

Mortality data for the Norwegian population (1999–2010) in 1-year age groups was obtained from Statistics Norway [15].

Statistics

The data were analyzed in Stata 12. Median survival time (time at which survival probability is 0.5) with 95% confidence intervals was estimated. Absolute mortality rates were analyzed by Cox proportional hazard regression adjusted for age. Standardized mortality rates (SMRs) with 95% confidence intervals were calculated separately for women and men with the mean mortality in the Norwegian population (1999–2008) in 5-year age groups as the reference. SMRs were calculated as an overall estimate, for specific survival times and for the age groups 50–64, 65–79 and 80+ years. An SMR of greater than 1 indicates that, after adjusting for the effect of differences in age between the groups, there is a higher mortality rate in patients with hip fractures than in the general population of Norway.

Based on population mortality, expected numbers of deaths were calculated and Poisson regression analyses were used to estimate SMRs in women and men by age groups (50–64, 65–79 and 80+ years).

Population attributable fracture fraction and years of potential life lost

Population attributable fraction (PAF) (1999–2008) was calculated by subtracting the sum of deaths and time at risk in hip fracture patients (up to 2 years after fracture) from the number of deaths and population at risk in Norway, to obtain mortality in a "non-hip-fracture population". The Norwegian population data was compared with the "non-hip-fracture population" in Poisson regression analyses. Years of potential life lost (YPLL) following hip fractures sustained between 1999 and 2008 were calculated in 1-year age groups based on expected remaining life years from Statistics Norway for the year 2008 [15].

Time trends in excess mortality

For the time trend analyses the hip fracture data were merged with year- and age-specific (1-year age groups) mortality data in the Norwegian population (1999–2008). 1-Year age-standardized absolute mortality rates in the hip fracture patients by calendar year were calculated and plotted. The expected number of deaths was calculated based on population mortality and Poisson regression analyses were used to test for time trends in SMRs (1-year mortality). Additional analyses were stratified by age groups 50–64 years, 65–79 years and 80 years and older.

Ethics

The study and the linkages of data were approved by the Norwegian Data Inspectorate, the Directorate of Health, Statistics Norway, and the Regional Committee for Medical and Health Research Ethics.

Results

Between 1 January 1999 and 31 December 2008, 81,867 (563/100,000) Norwegians in the population 50 years and older sustained their first hip fracture. Mean age at first hip fracture was 81.4 years in women and 78.7 years in men. Among the hip fracture patients, 37,411 women and 17,121 men died during the 12 years of follow up (1999–2010). The estimated median survival time was 4.2 (95% CI: 4.2–4.3) years in women and 2.6 (95% CI: 2.5–2.7) years in men. The overall SMRs in hip fracture patients compared to the Norwegian population were 2.5 (95% CI: 2.5–2.6) in men and 1.8 (95% CI: 1.8–1.8) in women. Hence, the age-adjusted SMR was 1.3 (1.3–1.4) times higher in men compared to women.

Mortality by time after first hip fracture in women and men

The greater excess mortality in men compared to women peaked in the first year post fracture but decreased over time (Table 1). During the first year following hip fracture, SMRs decreased gradually in both genders (Table 1). During the first year after the hip fracture 7836 men (33%) and 12,153 women (21%) died (Table 2). In hip fracture patients, 1-year mortality was almost five times higher in men and three times higher in women compared to the general Norwegian population.

Analyzing the data in 1-week intervals, the very highest excess mortality was observed in the first two weeks post fracture with SMR = 17.7 in men and 9.2 in women (Table 1). After two weeks, mortality declined in both genders (Table 1).

The highest excess mortality in both genders persisted during the first year after the hip fracture, with a significantly higher mortality in men (Table 1). Moreover, despite a decrease in mortality over time post-fracture, significantly increased excess mortality was observed in the 10th and 11th year after the fracture in both genders (Table 1).

Table 1
Standardized mortality ratios (SMRs) in women and men by time after the first hip fracture. The NORwegian EPidemiologic Osteoporosis studies.
The NOREPOS study.

	Time after hip fracture	No. of deceased	Expected[a]	SMR[b]	95% CI for SMR	
Men	First two weeks	1607	91	17.7	16.8	18.5
	0–3 months	4684	461	10.2	9.9	10.5
	3–6 months	1354	386	3.5	3.3	3.7
	6–12 months	1779	685	2.6	2.5	2.7
	1–3 years	4704	2197	2.1	2.1	2.2
	3–5 years	2498	1274	2.0	1.9	2.0
	5–10 years	1942	1104	1.8	1.7	1.8
	10–12 years	92	61	1.5	1.2	1.9
Women	First two weeks	1835	199	9.2	8.8	9.6
	0–3 months	6491	1093	5.9	5.8	6.1
	3–6 months	2400	985	2.4	2.3	2.5
	6–12 months	3203	1824	1.8	1.7	1.8
	1–3 years	10,795	6644	1.6	1.6	1.7
	3–5 years	7219	4454	1.6	1.6	1.7
	5–10 years	6677	4347	1.5	1.5	1.6
	10–12 years	311	241	1.3	1.2	1.4

[a] Expected number of deceased compared to the Norwegian population.
[b] Standardized mortality ratio after hip fracture.

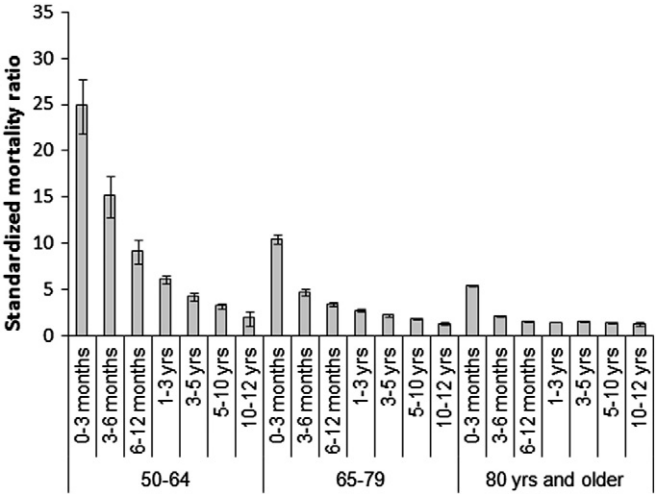

Fig. 1. Standardized mortality ratios with 95% confidence intervals in hip fracture patients by time after first hip fracture and age at first fracture for women and men combined. Mean mortality rates (1999–2008) for women and men combined in the Norwegian population (used to calculate SMRs) were 5.5, 25.6 and 114.2 per 1000 person years in the age-groups 50–64, 65–79 and 80 years and more, respectively.
The NORwegian EPidemiologic Osteoporosis studies.

Differences in mortality by gender and age

Age-adjusted mortality post hip fracture was higher in men than in women in all age groups studied ($p < 0.001$). In hip fracture patients who were 65 years and older, men had higher excess mortality than women. In the age group 50–64 years, SMR was significantly lower in men compared to women (RR = 0.9, $p = 0.01$).

Although SMRs were highest in the youngest, the burden in absolute terms was highest in those 80 years and older, among which 44% of men and 26% of women were dead within one year after the fracture (Table 2). Declining excess mortality by time after fracture was observed in all age groups. The highest excess mortality was observed in the age group 50–64 years with SMRs >20 (Fig. 1). In the younger age groups (younger than 80 years), there was a stepwise decline in mortality over time whereas in the oldest age group the SMRs appeared more flat 3-months after the hip fracture.

Population attributable risk and years of potential life lost

Overall, PAF of hip fracture to population mortality was 4.2% (95% CI: 3.5–4.9) in men and 5.1% (95% CI: 4.5–5.8) in women. In the age group 80 years and older at the time of fracture, the corresponding estimates were 6.0% (95% CI: 5.0–7.0) in men and 5.6% (95% CI: 4.8–6.4) in women. In men, most life-years were lost in the age group 65–79 years, whereas in women most life-years were lost above the age of 80 years (Table 3).

Time trends in 1-year mortality after first hip fracture

During the time-period 1999–2008, 1-year age-adjusted mortality rates in men with hip fracture declined by 12.1% (95% CI: 5.1–18.6). By contrast, there was no significant decline in age-adjusted mortality rates in women with hip fracture (Fig. 2). However, if excluding the 2008-data in women, there was a significant decline in mortality post hip fracture during the time period 1999–2007 ($p = 0.001$). In comparison, over the same period the mortality in the general Norwegian population of 50 years and older declined by 23.7% in men and 18.2% in women. Excess mortality in men did not change over time ($p_{timetrend} = 0.48$). As a result of the different mortality trends in women with and without a hip fracture, the excess 1-year mortality post hip fracture in women increased by 10.9% (95% CI: 1.3–21.5) between 1999 and 2008. This increase in excess 1-year mortality in women was significant only in the age group 65 years and older ($p_{timetrend} = 0.04$).

Discussion

In this study including nationwide data on more than 80,000 first hip fractures in Norway, the highest excess mortality was observed during the two first weeks following the fracture. Although excess mortality decreased by time after the hip fracture, it remained higher than in the general population throughout the 12 years after the fracture. At

Table 2
One-year mortality in Norwegian hip fracture patients by age at first fracture.
The NORwegian EPidemiologic Osteoporosis studies.

	Age at hip fx	No. of with hip fx	No. of deceased within 1-year	% dead within 1-year	Expected[a]	SMR[b,c]	95% CI for SMR	
Men	50–64	2805	264	9	22	11.9	10.6	13.4
	65–79	7977	1846	23	288	6.4	6.1	6.7
	80+	12,980	5726	44	1382	4.1	4.0	4.2
	Total	23,762	7836	33	1692	4.6	4.5	4.7
Women	50–64	3528	255	7	18	14.5	12.8	16.4
	65–79	16,434	2053	12	378	5.4	5.2	5.7
	80+	38,143	9845	26	3890	2.5	2.5	2.6
	Total	58,105	12,153	21	4286	2.8	2.8	2.9

[a] Expected number of deceased compared to the Norwegian population.
[b] Standardized mortality ratio.
[c] Adjusted for age in a Poisson model.

Table 3
Years of potential life lost after hip fracture.
The NORwegian EPidemiologic Osteoporosis studies.

	Age at fracture	No. of dead (after hip fx)	Years lost (1999–2008)
Men	50–64	836	16,200
	65–79	5102	42,204
	80+	11,151	34,687
Women	50–64	797	18,181
	65–79	7923	75,514
	80+	28,601	95,841

any time interval after the incidents, men had higher excess mortality than women. Between 1999 and 2008, the absolute 1-year mortality rates after hip fracture declined in men but not in women, and the excess mortality in the same period was unchanged in men, but increased by 11% in women. Including mortality up to two years post fracture, approximately 5% of the general mortality in Norway among persons 50 years or older could be attributed to hip fracture-related mortality.

Excess mortality by time after first hip fracture

Excess mortality during the first months after a hip fracture is well known. A meta-analysis indicated a hazard ratio of all-cause mortality in hip fracture patients compared with controls of 8.0 (95% CI: 6.1–10.3) in men and 5.8 (95% CI: 4.9–6.7) in women during the first 3 months after the hip fracture [3]. These are supported by the SMRs observed in the current study of 9.9 in men and 5.8 in women. Contrary to most other studies, we had the possibility to investigate mortality after fracture in smaller intervals than months. When using one-week intervals, the mortality peaked in the first two weeks and declined gradually over time in both genders thereafter. The high early mortality might be associated with complications after the hip fracture such as cardiovascular or infective causes as suggested by Cameron et al. [16]. The authors found that cardiovascular and infective diseases were the most important causes of death in the first 9 months post fracture. Therefore, it might be that there are different risk factors for early versus late mortality.

The decline in SMRs over time appeared steeper in the younger compared to the older age-groups. However, absolute mortality was much higher in the oldest compared to the youngest age-groups. Therefore, a decline in SMRs in the youngest age groups does not mean the same in absolute terms in the oldest patients. Anyway, the different time patterns in SMRs according to age might indicate different causes of death also according to age, but this needs further investigation.

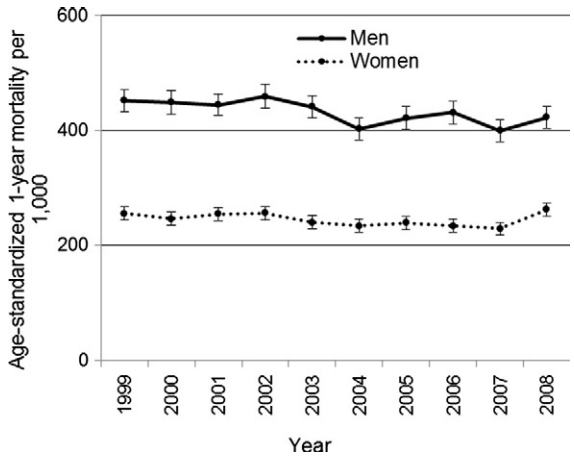

Fig. 2. Age-standardized 1-year mortality post hip fracture by calendar year.
The NORwegian EPidemiologic Osteoporosis studies.

In the current study, mortality remained significantly higher compared to the general population twelve years after the hip fracture, which is in accordance with the findings in the meta-analysis by Haentjens et al. [3]. We could, on the other hand, not confirm the analysis of Scottish National data indicating that mortality in hip fracture patients aged >85 years returned to the level of the background population between two and five years after fracture [17]. The published studies vary in study designs and populations, and this may affect estimates of both short- and long-term mortality [3,4]. Another possible explanation for the inconsistent findings could be related to differences in life expectancy between populations.

Gender differences in excess mortality after hip fracture

In the current study, men younger than 65 years had significantly higher absolute mortality rates compared to women, whereas excess mortality was significantly higher in women than in men in this age group. This contradicts earlier studies [3,18–20] reporting an excess mortality in men compared to women at any given age. As our dataset is based on hospitalizations for hip fracture, we cannot exclude hip fractures caused by excessive force. In the Harstad study, mean age at hip fracture differed significantly depending on place of fracture, with the highest mean age in nursing homes and the lowest outdoors [21]. Thus, one possible explanation for the lower SMR in men compared to women in the age group 50–64 years could therefore be that the younger hip fracture patients constitute a different population. On the other hand, the majority of young patients with hip fracture have a history of low-energy trauma [22].

Reasons for the differences in excess mortality between men and women after age 65 are not known. Multi-morbidity and high ASA score are related to increased risk of dying within the first year after fracture in some studies, but gender differences cannot be easily explained by differences in known comorbidity and medications [23,24]. Frost et al., who analyzed excess mortality attributable to hip fracture, reported that there was no significant effect of co-morbidity on the post-hip fracture relative survival [25]. In a register-based study from Denmark, Vestergaard et al. report that post fracture conditions such as infections and psychiatric conditions, and not pre-fracture co-morbid conditions, were responsible for the excess mortality in hip fracture patients [26]. Another study reported that infective causes of death, at least as recorded in death certificates, were largely responsible for the observed gender difference [7]. However, it should be remembered that there is a discrepancy between the health and survival of the genders in general. Men tend to be physically stronger and have fewer disabilities, but have substantially higher mortality at all ages compared to women [27].

Attributable risk and potential life-years lost post hip fracture

In the population aged 50 years and older, mortality associated with hip fracture during the first two years contributed in men 4.2% and in women 5.1% to the total population mortality, respectively. Hence, if hip fracture patients did not have excess mortality, the overall mortality in Norwegians aged 50 years and older would be 4% lower in men and 5% lower in women. Including the excess mortality persisting up to 12 years post fracture would have yielded even higher estimates. However, not all years lost after a hip fracture may be due to the hip fracture per se [28], and therefore we only included mortality up to two years post fracture. To put the results in perspective, a recent Japanese study [29] concluded that in women aged 60–75 years, tobacco smoking and high blood pressure contributed to 8% and 7% of the total mortality, size effects comparable to our estimates. This comparison illustrates the magnitude of the hip fracture related mortality and shows, as in a Finnish study from 2008 [19], that hip fracture is a powerful independent predictor of long-term excess mortality in both genders, with higher effect in men.

Another approach for estimation of burden of disease is to calculate life-years lost. As demonstrated in this study, most hip fracture related life-years were lost in men aged 65–79 years, whereas in women a similar proportion of life-years were lost in those women aged 50–79 at the time of fracture as in women 80 years and older. Norway has one of the world's highest reported incidences of hip fractures [30,31], and as these analyses show, the potential for prevention of hip fracture related mortality is also very high.

Time trends

In the current study, mortality rates among men with a hip fracture decreased by 12% between 1999 and 2008, whereas excess mortality in the same period did not change significantly. In women, the opposite was observed; mortality rates were unchanged but, due to decreasing population mortality rates, excess mortality increased significantly. The latter findings are consistent with a Danish study showing an increase in excess mortality among hip fracture patients between 1981 and 2001 [12]. In an American study, hip fracture mortality decreased significantly in men, but not in women between 1990 and 2007 [10]. Possible reasons for the conflicting results include comparative data not being collected in the same time periods [6–9], mortality rates in the general population not being similar across countries, hip fractures not being captured equally within all socioeconomic groups, hip fracture rates varying between countries and different methodology being used to collect data.

Strengths and limitations

The present study is based on a large nationwide dataset of validated hip fractures with 12 years of follow-up. The dataset includes date of hip fracture and date of death for all hip fracture patients treated in Norwegian hospitals during the period, enabling the calculation of exact number of follow-up days for the entire hip fracture population. Calculated incidence rate ratios (data not shown) were very similar to the standardized mortality ratios.

Years of potential life lost were based on expected remaining life-years and mean survival in the hip fracture patients. Data from 1999 to 2008 were used in the calculations, but those who fractured near the end of the study did not have the same possibility to contribute to the mean survival time. As a result the estimates might be overestimated, but nevertheless they give important information about the age-distribution of life-years lost.

A second hip fracture is followed by an even higher mortality than the first hip fracture [32,33]. To minimize second hip fractures being incorrectly considered as a first fracture, we excluded the first five years of the observation period (1994–1998). However, we have estimated that this misclassification is likely to comprise less than 5% of the hip fractures and due to the high numbers this probably did not influence our findings [14].

Conclusion

Excess mortality remains increased more than 10 years after a hip fracture in both men and women. The first three months after the hip fracture is the most vulnerable period with the highest risk of death, especially in the age groups up to the age of 80 years. In total, hip fractures contributed 4% in men and 5% in women to population mortality. The largest part of the life-years lost were in the relatively young-old. Hip fractures remain an important target for improved prevention and treatment.

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Conflict of interest

The authors declare that they have no conflict of interest.

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