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REVIEW

Excess mortality following hip fracture: a systematic epidemiological review

B. Abrahamsen · T. van Staa · R. Ariely · M. Olson · C. Cooper

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Abstract *Summary* This systematic literature review has shown that patients experiencing hip fracture after low-impact trauma are at considerable excess risk for death compared with nonhip fracture/community control populations. The increased mortality risk may persist for several years thereafter, highlighting the need for interventions to reduce this risk.

Patients experiencing hip fracture after low-impact trauma are at considerable risk for subsequent osteoporotic fractures and premature death. We conducted a systematic review of the literature to identify all studies that reported unadjusted and excess mortality rates for hip fracture. Although a lack of consistent study design precluded any formal meta-analysis or pooled analysis of the data, we have shown that hip fracture is associated with excess mortality (over and above mortality rates in nonhip fracture/community control populations) during the first year after fracture ranging from 8.4% to 36%. In the identified studies, individuals experienced an increased relative risk for mortality following hip fracture that was at least double that for the age-matched control population, became less pronounced with advancing age, was higher among men than women regardless of age, was highest in the days and weeks following the index fracture, and remained elevated for months and perhaps even years following the index fracture. These observations show that patients are at increased risk for premature death for many years after a fragility-related hip fracture and highlight the need to identify those patients who are candidates for interventions to reduce their risk.

Keywords Excess mortality · Femoral neck fracture · Fragility-related fracture · Hip fracture · Osteoporotic hip fracture · Systematic review

B. Abrahamsen (✉)
Department of Internal Medicine and Endocrinology,
Copenhagen University Hospital Gentofte,
Niels Andersensvej 65,
2900 Hellerup, Denmark
e-mail: b.abrahamsen@physician.dk

T. van Staa
General Practice Research Database,
London, UK

T. van Staa
Utrecht Institute for Pharmaceutical Sciences, Utrecht University,
Utrecht, The Netherlands

R. Ariely
Novartis Pharmaceutical Corporation,
East Hanover, NJ, USA

M. Olson
Novartis Pharma AG,
Basel, Switzerland

C. Cooper
MRC Epidemiology Resource Centre,
University of Southampton,
Southampton, UK

C. Cooper
NIHR Biomedical Research Unit in Musculoskeletal Sciences,
University of Oxford,
Oxford, UK

Introduction

Hip fractures, defined as any fracture of the femur between the articular cartilage of the hip joint to 5 cm below the distal point of the lesser trochanter, can occur at any age but are most common in older persons [1, 2]. Most patients presenting with hip fracture are women aged over 50 years, and the mean age at first presentation is approximately 80 years [1, 2]. Johnell and Kanis estimated a worldwide incidence of 1.6 million osteoporotic fractures of the hip in people aged 50 years and older in 2000, of which about 70% (1.14 million) were in women [3]. The absolute global annual incidence of hip fracture is expected to increase to 2.6 million by 2025 and to 4.5 million by 2050 alongside an expanding and increasingly elderly population [4, 5].

Most cases of hip fractures arise because of low-impact trauma in an individual with underlying bone fragility. In individuals aged 50 years or older, 53% of all fractures are associated with low-impact trauma (generally arising from a fall), rising to 80% of hip fractures in those aged 75 years or older [6]. The bone fragility that places older persons at increased risk of fracture following a low-impact trauma is most often due to underlying osteoporosis, suggesting that hip fracture is almost always due to underlying osteoporosis.

It has been suggested that as many as one in three women and one in eight men over 50 years of age have osteoporosis [7]. Moreover, recent surveys suggest that even after a diagnosis of osteoporosis, which is usually precipitated by a fragility-related fracture, patients often do not receive the recommended or adequate treatment [8–10].

Particularly worrying in light of the low rate of diagnosis and lack of sustained intervention following diagnosis is the apparent considerable risk of mortality following hip fracture. The U.S. Congress Office of Technology Assessment (1994) estimated that an average of 24% of patients 50 years and older with hip fracture die in the year following their index fracture. Johnell and Kanis estimated that there were almost 750,000 deaths worldwide associated with hip fracture in people aged 50 years and older in 1990 [5]. Other studies have indicated that the community mortality rates associated with hip fracture may be higher than for other better known life-threatening conditions such as pancreatic or stomach cancer [11] and myocardial infarction [12].

Although mortality following hip fracture is apparently high, to our knowledge, there has been no systematic evaluation of the current evidence base with regard to excess mortality rates. We undertook a systematic review of the literature in order to better define the mortality risk faced by individuals experiencing hip fracture. We have examined both crude mortality rates and the excess mortality these patients face in relation to control populations with the aim of highlighting at-risk groups where active intervention could modify risk factors for excess mortality.

Methods

PubMed was searched in October 2008 using the following search terms: [hip fracture OR femoral neck fracture OR neck of femur] AND [death OR mortality OR survival]. The following restriction was applied: language English. The search covered titles and abstracts.

Noninterventional/nonrandomized observational, prospective, and retrospective studies were eligible for inclusion in this analysis. Excluded study types were interventional studies, case studies, and meta-analyses. Studies with populations <100, those examining mortality rates primarily focusing on patients with a pre-existing serious medical illness (such as myocardial infarction, Parkinson's disease, or renal dysfunction), and those not specific for hip fracture mortality were excluded. The outcome measures that were of particular interest were unadjusted mortality (the absolute, observed mortality rate within a defined study population) and excess mortality (mortality beyond that expected/observed for matched control/population groups) and the relative risk (RR) for death compared with control groups without fracture.

Statistical analyses

No formal meta-analysis was possible due to the lack of consistency in study design across the included studies. Descriptive statistics are presented throughout.

Results

The initial PubMed search returned a potential 1,114 studies for consideration. In all, 1,052 studies were discounted after the exclusion criteria were applied, including 15 studies that were nonspecific for mortality associated with hip fracture, 14 studies in which mortality was not the primary outcome, four studies in which participants had an a priori medical diagnosis, two studies that reported extrapolated rather than actual mortality estimates, and one population surveillance study that did not specifically report data for hip fracture. In all, 63 studies were considered suitable for inclusion in the present systematic analysis (Table 1). The majority of studies included samples from populations older than 50 years, with a mean age of approximately 80 years. Subjects were mainly female and had largely been treated surgically. The studies had mostly been conducted in the USA or Europe, with additional studies reported for Japanese, Australian, and New Zealand populations.

A total of 54 studies presented unadjusted mortality data (deaths as a proportion of the study population; Table 2). These studies were conducted in Argentina, Australia, Canada, Denmark, Finland, France, Greece, New Zealand, Norway, Singapore, Spain, Sweden, The Netherlands, UK, and USA. Cumulative unadjusted mortality rates increased over time following the index fracture, from 2.3–13.9%

during the index hospitalization to 5.9–50% up to 1 year after the fracture.

In all, 22 studies reported excess mortality rates compared with local population norms (Table 3). The studies were conducted in northern Europe (Sweden, Denmark), France, Germany, New Zealand, UK, and USA. Excess mortality rates compared with population-controlled cohorts (including general population rates) during the first year post-fracture were reported in 12 studies [13–24] and ranged from 8.4% in a Swedish population [13] to 36% in the USA [18].

Five studies reported an RR analysis for death following hip fracture and four other studies reported mortality hazard ratios (HRs) [13, 19, 21, 22, 24, 25–28]. The study by Wolinsky and co-workers reported a mortality risk analysis following hip fracture relative to institutionalized elders without hip fracture rather than relative to a general age-matched population [24]. Overall, the risk of mortality following hip fracture was at least double that for age-matched population values (Fig. 1).

Temporal profile of post-fracture mortality

Unadjusted mortality rates over time

The cumulative mortality rate over the first 12 months after hip fracture ranged from 5.9% among US patients aged 50–74 years (deaths identified via the mortality listings from the Vital Records Section of the Washington State Department of Social and Health Services) [23] to 50% among all patients admitted to a single US hospital for hip fracture between 1956 and 1961 [29] (Table 2). The inpatient mortality rate following hip fracture ranged from 2.3% among women attending a US urban orthopedic referral hospital [30] to 13.9% in patients treated at a single hospital in Norway [31].

Twelve studies examined the accumulation of mortality up to 1 year after fracture [13, 15, 32–41]. Of these, four studies reported mortality rates at 1 and 12 months post-fracture, all of which found that between one-quarter and one-third of the observed mortality occurred in the first month after fracture [34, 35, 37, 41]. Seven studies indicated that around half of the observed mortality occurs within the first 3 months post-fracture [15, 32, 33, 36, 38–40], with four studies indicating that around 70% of all observed deaths had occurred by 6 months post-fracture [13, 32, 38, 40].

Mortality risk over time

In the five studies that evaluated mortality risk over time, the highest risk of death was in the first 6 months after fracture [19, 21, 24, 25, 42] (Table 3). A standardized mortality ratio (SMR; observed/expected deaths) of 6.0 was calculated for the first 6 months after hip fracture among women in France compared with nonfracture controls matched for age and baseline health status and a history of falls; the SMR fell to 2.0 after 6 months [25]. Using a Cox proportional hazards model, Tosteson and co-workers found that hip fracture patients were 11.6 times more likely to die than controls within the first 6 months post-fracture after adjustment for age, sex, and race, with the risk reducing to 1.37 times that of controls thereafter [21]. In this study, the excess mortality risk was no longer significant beyond 6 months after adjustment for age, sex, race, prefracture functional status, socioeconomic status, facility residence, body mass index, comorbid conditions, and overall health status. Two studies utilized data from the Longitudinal Study of Aging to determine excess risk over time. Magaziner and co-workers compared 529 white, female community-dwelling hip fracture patients aged >70 years with 3,773 gender- and aged-matched nonhip fracture participants in the Longitudinal Study of Aging [42]. The authors determined an expected mortality rate for the nonhip fracture population (using a Cox regression analysis) and compared this with observed mortality rate among participants with hip fracture. In the first 2 months after fracture, the observed/expected ratio was 6.08, indicating an excess mortality, decreasing to 1.29 between months 6 and 12 post-fracture, and returning to equality (1.0) thereafter.

Wolinsky and co-workers found that the mortality risk was greatest during the first 6 months after fracture in their population of 368 participants aged >70 years in the Longitudinal Study of Aging compared with 7,159 age-matched participants in the same study [24]. They calculated an adjusted HR of 38.93 (95% confidence interval [CI], 29.58–51.23) for the first 6 months post-fracture compared with an adjusted HR of 1.17 (95% CI, 0.95–1.44) for the subsequent 7.5-year observation period (Table 3).

Rapp and co-workers examined the mortality risk following hip fracture among a population of >69,000 elderly people newly admitted to German nursing homes [19]. Using sex, age, and level of care-matched nursing home residents as the control group, they found that excess mortality was limited to the first 3 months post-fracture for women and the first 6 months post-fracture for men (HR women, 0–3 months 1.72 [95% CI, 1.59–1.86], >3–6 months 1.00 [95% CI, 0.89–1.13]; men, 0–3 months 2.14 [95% CI, 1.80–2.53], >3–6 months 1.40 [95% CI, 1.08–1.82]).

Farahmand and co-workers reported an RR of just under three times (2.7) that of the Swedish population in the 12 months post-fracture, with an RR of just over three times (3.3) that of the Swedish population in the first 6 months post-fracture [13]. Dahl and co-workers reported a mortality

Table 1 Overview of studies included in this analysis

Study	Geographical location	Study type	Timeframe	Population	Sample[a]	Gender	Mean age at fracture (years)
Allaf and Lovell [32]	UK	Database	1996–2001	Patients admitted to hospital following hip fracture	1,314	–	–
Aharanoff [99]	USA	Prospective	1987–1993	Consecutive admissions for nonpathological hip fracture; >65 years of age	612	80% female	–
Bass [33]	USA	Database	1999–2002	Elderly veterans with hip fracture	43,165	87% men	80
Bass [100]	USA	Database	1998–2002	Veterans Health Administration patients	13,546	Primarily men	–
Beals [29]	USA	Prospective	1956–1961	Patients with hip fracture	248 FFN (total, 607)	Women/men ratio 2.5:1	–
Benet-Travé [46]	Spain	Prospective	1991	Patients >65 years	1,222 FFN (total, 2,870)	76.9% women	Women, 80.9 Men, 79.9
Bjørgul and Reikerås [34]	Norway	Prospective consecutive cohort	1998–2003	Patients >60 years with hip fracture	466	–	
Boereboom [49]	The Netherlands	Prospective	1982–1984	Consecutive hip fracture patients aged ≥50 years	493	79.1% women	Women survivors, 73.9 Women nonsurvivors, 82.3 Men survivors, 69.1 Men nonsurvivors, 78.0
Boufous [65]	Australia	Database	1990–2000	Patients >50 years admitted to hospital for hip fracture	–	–	–
Cipitria [50]	Argentina	Retrospective	1979–1995	Patients >50 years with hip fracture	200	77% women	Women, 79.3 Men, 78.7
Cree [48]	Canada	Prospective inception cohort	1996–1997	Patients >64 years admitted to hospital for hip fracture	558	74% women	81
Dahl [31]	Norway	Prospective	1961–1970	Patients with hip fracture	675	74.1% women	73.9 Women, 71.5 Men, 74.7
Deakin [35]	UK	Database	2001–2005	All patients with fractures of the limbs and pelvis	2,888 FFN (total, 8,834)	–	–
Eastwood [101]	USA	Prospective	1997–1998	Patients ≥50 years hospitalized following hip fracture	571	81% women	81.8
Empana [25]	France	Prospective		Ambulatory elderly women >75 years	338 (controls, 7,174)	100% women	–
Endo [30]	USA	Retrospective analysis of prospectively collected data	1987–2000	Patients ≥65 years with hip fracture who underwent operative treatment	983	79% women	Men, 80.1 Women, 79.6
Farahmand [13]	Sweden	Database	1993–1995	Women aged 50–81 years	2,245 (controls, 4,035)	All women	73.3
Fisher [36]	USA	Database	1984–1986	Patients >65 years with osteoporotic hip fracture	22,039	79.8% women	–
Forsén [26]	Norway	Prospective matched-pair cohort	1986–1995	Adults >50 years hospitalized following hip fracture	1,825 (controls, 19,227)	73.3% women	

Fransen [14]	New Zealand	Cohort	1991–1996	Community-dwelling patients >60 years	548 (controls, 760)	74.1% women	–
Giversen [15]	Denmark	Retrospective cohort	1987–1996	Patients ≥50 years experiencing a first hip fracture	2,674	–	–
Goldacre [102]	UK	Database	1994–1998	Patients ≥65 years admitted to hospital for FFN	8,148	80% women	82.2
Hasegawa [56]	Japan	Prospective follow-up	2000	Patients ≥50 years	759	72% women	80
Heikkinen [103]	UK and Finland	Observational database	1989–1997	All patients ≥50 years with hip fracture	3,785	–	UK, 80.3 Finland, 78.3
Hindmarsh [51]	Australia	Population-based cohort	2000–2003	Patients >65 years with hip fracture	16,836	75% women	–
Holt [47]	UK	Database	1998–2005	Scottish Hip Fracture Audit participants >50 years	25,649	78% women	Women, 81 Men, 77
Holt [60]	UK	Database	1998–2004	Scottish Hip Fracture Audit participants	18,817	78.9% women	–
Jiang [45]	Canada	Population-based cohort	1994–2000	Patients ≥60 years with hip fracture	3,981	71% women	82
Johnell [27]	Sweden	Database	1990–1991	All recorded hip fractures	1,143 (total, 2,847)	–	–
Kanis [11]	Sweden	Database	1987–1996	Patients ≥50 years on the Swedish patient register	158,589	73% women	–
Kernek [104]	USA	Retrospective	1946–1955 and 1982–1986	Patients with hip fracture treated surgically at a single center	879	84.4% women	72
Kreutzfeldt [62]	Denmark	Prospective	1978	Community dwellers aged >60 years	117	–	–
Lawrence [37]	USA	Retrospective cohort	1982–1993	Consecutive patients ≥60 years requiring surgical repair for hip fracture	8,930	79% women	80.2
Magaziner [42]	USA	Prospective	1984–1986	Community-dwelling white hip fracture patients	529 (controls, 3,773)	All women	81.6
McColl [105]	UK	Database	1993–1995	Patients >65 years admitted to hospital following hip fracture	3,145	–	–
Miller [57]	USA	Retrospective	1972–1974	Patients with hip fracture	360	71% women	73
Mortimore [61]	USA	Prospective	1990–1991	Baltimore Hip Study cohort >65 years	674	77.4% women	81.1
Mullen and Mullen [54]	USA	Prospective	1981 onwards	Consecutive hip fracture cases	400	–	–
Myers [52]	USA	Database	1979–1988	Patients >65 years with hip fracture	27,370	80% women	Women, 81 White men, 79 Black men, 76
Nather [38]	Singapore	Retrospective	1990–1992	Patients >60 years with hip fracture	110	83.6% women	78
Paksima [16]	USA	Prospective	1987–2003	Patients >65 years with hip fracture	1,109	78.8% women	–
Parker and Anand [17]	UK	Prospective	Not specified	Consecutive patients with hip fracture	703	82% women	Women, 80 Men, 74
Petitti and Sidney [55]	USA	Database	1980–1984	Women >49 years with hip fracture	2,048	All women	–
Poór [18]	USA	Population-based cohort	1978–1989	Men with first nonpathological hip fracture	131 (controls, 131)	All men	79.2
Radcliff [106]	USA	Database	1998–2003	Veterans Affairs database, aged >65 years	5,683	All men	–
Rapp [19]	Germany	Retrospective cohort	2000–2005	Institutionalized elders aged ≥65 years	4,342 (controls, 17,368)	86.6% women	Women, median 85.2, Men, median 81.5
Richmond [43]	USA	Retrospective analysis of prospectively collected data	1987–1997	Previously ambulatory Caucasian adults ≥65 years	836	79% women	79.8
Roberts and Goldacre [39]	UK	Database	1968–1998	Patients aged ≥65 years admitted to hospital following hip fracture	32,590	82% women	81.5

Table 1 (continued)

Study	Geographical location	Study type	Timeframe	Population	Sample[a]	Gender	Mean age at fracture (years)
Roos [53]	Canada	Database	1979–1992	Patients ≥65 years admitted for surgical repair of hip fracture	Manitoba, 10,007 New England, 16,206	75.1% women	–
Rosencher [67]	France	Observational follow-up	2002	Patients ≥18 years undergoing hip fracture surgery	6,860	76% women	82
Schrøder and Erlandson [40]	Denmark	Prospective	1970–1985	Patients ≥40 years with hip fracture	3,895	Female/male ratio 2.7:1	Women, 78 Men, 74
Sexson and Lehner [20]	USA	Retrospective	1980–1983	Elders with hip fracture	300	77.3% women	–
Shah [59]	USA	Prospective	1987–1996	Consecutive community-dwelling patients ≥65 years treated surgically for hip fracture	850	79% women	79.7
Stavrou [72]	Greece	Retrospective	1990–1994	Patients admitted to an orthopedic department for nonpathologic hip fracture	202	74% women	76
Tosteson [21]	USA	Retrospective analysis of prospectively collected data	1996–2000	Participants in the Medicare Current Beneficiary service aged ≥65 years	730 (Controls: 24,448)	74% women	–
Tsuboi [44]	Japan	Prospective	1992	Patients >50 years with hip fracture	753	74.6% women	78.2
Van de Kerkhove [63]	The Netherlands	Retrospective	1982–2001	Patients ≥90 years with hip fracture	155	82.6% women	–
Vestergaard [28]	Denmark	Historical cohort	1977–2001	Danish population	169,145 cases (controls, 524,010)	72% women	77.0
Verstergaard [22]	Denmark	Historical cohort	1981 versus 2001	Danish population	163,313 cases (controls, 505,960)	72% women	–
Walker [41]	New Zealand	Database	1988–1992	Patients >60 years admitted to hospital following hip fracture	10,684	78% women	–
Weiss [23]	USA	Prospective	1976–1979	Females with hip fracture	168 (total, 385)	All women	–
Wolinsky [24]	USA	Longitudinal follow-up	1984–1991	Elders >70 years with hip fracture	368 (controls, 7,159)	78% women	79.7
Wood [58]	UK	Prospective	1982 onwards	Patients with hip fracture	531	80.8% women	77.5

[a] Sample size indicates the total number of hip fracture patients included in the study; total study populations (if different) or the number of control patients (where available) are given in brackets

FFN fractured femoral neck

rate 15 times greater than for the general Norwegian population in the first month post-fracture and seven times greater in the second month [31]. Thereafter, for up to 4 years post-fracture, they found that the mortality rate was comparable with that for the general population.

Duration of increased mortality risk

Twelve studies examined the duration of the mortality risk in the years following hip fracture [11, 14, 16, 19, 21, 24, 25, 27, 28, 36, 43, 44]. Nine of the 12 studies reported that patients face an increased risk of death for several years following a hip fracture.

Two studies examined the mortality risk for up to 2 years following the index hip fracture [14, 43]. The risk of death at 2 years after an index hip fracture was 1.34 (95% CI, 0.83–2.16) in women and 7.18 (95% CI, 2.04–21.99) in men in one study [14], with an SMR at 2 years of 1.4 ($p<0.001$ versus expected) reported in the second study [43]. Fisher and co-workers found that among a cohort of Medicare users in the USA, the excess risk for death among patients with hip fracture persisted for up to 3 years post-fracture [36]. At 5 years post-hip fracture, the mortality rate among men and women was significantly higher than for age-matched general population cohorts for all 5-year age groups from 50 to 90 years [11]. In a Japanese population, the mortality rate remained higher for individuals following hip fracture compared with the general population for up to 10 years after the index fracture [44]. Forsén and co-workers followed patients for up to 9 years after their index fracture [26]. They found that both men and women <75 years old experienced a 2- to 3-fold excess risk of death for at least 6.5 years for women and 5 years for men. Similarly, Paksima and co-workers reported that the excess SMR for patients aged 65–84 years persisted for up to 10 years post-fracture among a cohort of 1,109 patients with hip fracture admitted to a single US hospital [16]. Consistent with this, Johnell and co-workers found that the RR for death following hip fracture remained higher than among the general population for both men and women up to 5 years post-fracture [27]. Finally, the study reported by Vestergaard and co-workers suggested that the risk of death may persist for at least 20 years after the index fracture [28]. However, as noted above, in the study reported by Tosteson and co-workers, in which patients were followed for a median of 1.5 years after fracture, the excess mortality risk was no longer significant beyond 6 months after adjustment for age, sex, race, prefracture functional status, socioeconomic status, facility residence, body mass index, comorbid conditions, and overall health status [21]. Wolinsky and co-workers also found that the excess mortality was limited to the first 6 months post-fracture among patients aged >70 years who took part in the US-based Longitudinal Study of Aging [24]. Finally, Rapp and co-workers found that the excess mortality faced by institutionalized elders with hip fracture compared with institutionalized elders without hip fracture was also limited to the first 6 months post-fracture [19].

Hip fracture mortality and gender

Unadjusted mortality rates

The unadjusted mortality rates following hip fracture support a gender bias in favor of women both during the index hospitalization and in the months and years following the index fracture.

In a retrospective US analysis, the mortality rate in men was almost twice that in women while in hospital following hip fracture (unadjusted rate 4.3% versus 2.3% for women) [30]. The study also found that men had a higher preoperative risk (according to the American Society of Anesthesiologists' classification system) and were more likely to experience at least one postoperative complication. Similarly, Jiang and co-workers observed a significantly higher risk of inpatient mortality among men than in women (10.2% versus 4.7%; $p<0.001$), a dichotomy that became more pronounced with advancing age so that for patients older than 90 years, inpatient mortality for men was 17.5% compared with 8.7% for women ($p=0.01$) [45]. A significantly higher case fatality rate for males compared with females (males 11.9% versus females 5.3%; $p<0.001$) was also reported by Benet-Travé and co-workers in their analysis of in-hospital mortality following hip fracture in a Spanish population [46]. Beals found that the in-hospital mortality rate was higher among males over 70 years compared with younger patients [29].

Studies of the mortality rates in the first year following hip fracture confirm a disparity between male and female patients. Within 1 month of the index fracture, the mortality rate among men was 17.1% compared with 9.8% for women ($p<0.01$) in a Norwegian patient population [31] and men were less likely to survive to 30 days post-fracture in a large UK population (30-day mortality rate: men 12%, women 7%; odds ratio [OR] 1.93; 95% CI, 1.73–2.14) [47]. At 3 months post-fracture, the mortality rate for men was higher than in women (13% versus 6%) among Canadian hip fracture patients presenting at one of two acute care centers [48]. Several studies have reported that the increased mortality rate for men compared with women was still evident up to 1 year post-fracture [30, 32, 36, 45, 49–51]. Endo and co-workers reported that the increased risk of death for men versus women was still evident up to 1 year post-fracture (16.5% versus 9.4%; $p<0.01$), while Jiang and colleagues observed a mortality rate of 37.5% for men and 28.2% for women ($p<0.001$) after 1 year [30, 45].

Table 2 Unadjusted post-fracture mortality rates

Citation	Post-fracture mortality rate (%)					
	Sample size	In hospital	1 month	3 months	6 months	1 year
Allaf and Lovell [32]	1,314	–	8.47	–	–	–
Aharanoff [99]	612	3.9	–	6.5	8.8	12.7 Women, 10.7 Men, 20.7
Bass [33]	43,165		8.9	15.6	21.8	29.9
Bass [100]	13,546	Community hospitals, 3.3 Veterans Health Administration, 7.8	–	–	–	–
Beals [29]	248	9	–	–	–	50
Benet-Travé [46]	1,222	5.3	–	–	–	–
Bjørgul and Reikerås [34]	466	–	Undisplaced,7 Moderately displaced, 5	–	–	Undisplaced, 22 Moderately displaced, 25
Boereboom [49]	493	9.1	–	–	–	Men, 33 Women, 23.6
Boufous [65]	–	5.1	–	–	–	–
Cipitria [50]	200	–	–	–	–	Men, 13 Women, 9.1
Cree [48]	558	–	6.6	8	–	–
Dahl [31]	675	13.9	Men, 17.1 Women, 9.8	–	–	–
Deakin [35]	2,888	–	11.4	–	–	33
Eastwood [101]	571	–	–	–	13.5	–
Endo [30]	983	Men, 4.3 Women, 2.3	–	–	–	Men, 16.5 Women, 9.4 Overall, 11
Farahmand [13]	2,245	–	–	–	7.1	10.6
Fisher [36]	22,039	–	6.3	12.5	–	23.7
Forsén [26]	1,825	–	–	–	–	Men, 31 Women, 17
Giversen [15][a]	2,674	–	9	15.5	–	26.5
Goldacre [102]	8,148	3.5	4.5	6.9	7.7	–
Hasegawa [56]	759	–	3.3	–	–	–
Heikkinen [103]	3,785	–	–	–	–	UK, 27.1 Finland, 24.9
Hindmarsh [51]	16,836	–	–	–	–	21% attributable to hip fracture
Holt [47]	25,649	–	Men, 12 Women, 7	–	–	–
Holt [60]	18,817	–	7	–	–	–
Jiang [45]	3,981	6.3	–	–	–	30.8

Johnell [27]	1,143	–	–	–	–	22
Kernek [104]	1950, 727 1980, 386	–	1950, 13 1980, 4.2	–	–	–
Kreutzfeldt [62]	117	–	–	–	–	26.5
Lawrence [37]	8,930	–	4	–	–	16
McColl [105]	3,145	7	–	–	–	–
Miller [57]	360	11	–	–	–	27
Mullen and Mullen [54]	400	–	–	–	–	16
Myers [52]	27,370	4.9	–	–	–	–
Nather [38]	110	–	–	6.4	9.1	15
Paksima [16]	1,109	–	–	–	–	11.9
Parker and Anand [17]	709	–	–	–	–	15% attributable to hip fracture
Petitti and Sidney [55]	2,048	3.7	–	–	–	–
Poór [18]	131	–	–	–	–	42
Radcliff [106]	5,683	6.6	8	–	–	–
Richmond [43]	836	–	–	–	–	11.5
Roberts and Goldacre [39]	32,590	–	11.1	20.4	–	32.7
Roos [53]	1979–86, 4,674	–	7.4	–	–	–
	1986–1992, 5,333	–	7.9	–	–	–
	1984–1985, 16,206	–	5.5	–	–	–
Rosencher [67]	6,860	–	5.2	10.6	–	–
Schrøder and Erlandson [40]	3,895	–	9.5	16.8	21	27
Sexson and Lehner [20]	300	–	–	–	–	14.8
Shah [59]	850	2.8	–	–	–	10.9
Stavrou [72]	202	–	–	–	–	18
Tsuboi [44]	753	–	–	–	–	19
Van de Kerkhove [63]	155	Men, 7.4 Women, 12.5	Men, 8.3 Women, 17.2	–	–	–
Verstergaard [22]	169,145	–	–	–	–	28
Walker [41]	10,684	–	8	–	–	24
Weiss [23]	168	–	–	–	–	5.9
Wood [58]	531	–	–	–	23	–
Overall range		2.3–13.9	3.3–17.2	6.4–20.4	7.1–23	5.9–50

[a] Mortality rates estimated using a weighted regression analysis

Table 3 Relative mortality risk in hip fracture cases compared with nonhip fracture control populations

Citation (country)	Timeframe	Crude mortality rate		Excess mortality rate	Mortality risk (95% CI)	
		Cases	Controls			
Parker and Anand [17] UK	Up to 1 year post-fracture	Overall, 36.7%	6.3%	30%	Not reported	
		Men, 37.1%	6.0%	31.1%		
		Women, 36.6%	6.4%	30.2%		
Poór [18] USA	Up to 1 year post-fracture	42%	6%	36%	Not reported	
Sexson and Lehner [20] USA	Up to 1 year post-fracture	14.8%	3%	11.8%	Not reported	
Weiss [23] USA	Up to 1 year post-fracture	5.9%	1.5%	4.4%	Not reported	
	Up to 2 years post-fracture	10.5%	3.0%	7.5%	Not reported	
Kaplan–Meier survival curves and relative risk analysis						
Farahmand [13] Sweden	During first year post-fracture	10.6%	2.2%	8.4%	4.5 (3.5–5.8)	2.7 (2.1–3.4)
					Adjusted for age	Adjusted for age and previous hospitalization
	Within 6 months post-fracture	7.1%	1.1%	6%	5.7 (4.1–7.9)	3.3 (2.4–4.6)
					Adjusted for age	Adjusted for age and previous hospitalization
Forsén [26] Norway	Up to 1 year post-fracture (men/women)		Not reported	Not reported		
	Overall	31%/17%				
	50–74 years	16%/7%			4.2 (2.8–6.4)/3.3 (2.1–5.2)	
	75–84 years	30%/18%			2.9 (2.2–3.9)/2.5 (2.0–3.1)	
	>85 years	27%/48%			3.1 (2.2–4.2)/1.6 (1.2–2.0)	
	Up to 3 months post-fracture (men/women)	Not reported	Not reported	Not reported		
	50–74 years				9.0 (4.9–16.5)/5.2 (2.4–10.9)	
	75–84 years				5.1 (3.5–7.5)/5.9 (4.1–8.3)	
	>85 years				5.7 (3.4–9.6)/3.7 (2.5–5.4)	
Johnell [27] Sweden	At 1-year follow-up	22%	Not reported	Rate/1000 in men/women	Men/women	
	Aged 60 years			92.9/45.4	10.2/9.1	
	Aged 80 years			229/103	3.7/3.0	
Multiple logistic regression analyses to calculate adjusted odds ratios						
Fransen [14] New Zealand	At 2-year follow-up					
	Men	38.0%	8.2%	29.8%	7.18 (2.04–21.99)	
	Women	20.7%	10.3%	10.4%	1.34 (0.83–2.16)	
Poisson modeling						
Kanis [11] Sweden	At 1-year post-fracture		Not reported	Rate/1000 in men/women	Not reported	
	Aged 60 years			37.2/20.2		
	Aged 80 years			116.5/48.6		
	At 6 months post-fracture		Not reported	Rate/1000 in men/women	Not reported	
	Aged 60 years			47.1/24.5		
	Aged 80 years			157.4/64.9		
Mortality ratios[a]						
Empana [25] France	Rate/1000 woman-years	112.4	27.3	SMR	Relative risk	
				0–6 months, 6	3.3 (2.5–4.3)	
					Adjusted for hip fracture	
				>6 months, 2	2.6 (1.9–3.4)	
					Adjusted for hip fracture and age	
					2.1 (1.6–2.8)	
					Adjusted for age and baseline health status	

Goldacre [102] UK				SMR/100 patients	
				Month 1, 1246	
				Month 3, 451	
				Month 6, 238	
				Month 12, 187	
Magaziner [42] USA	1–2 months post-fracture			Observed/expected, 6.08	Not reported
	6–12 months post-fracture			1.29	
Paksima [16] USA			Not reported	SMR	Not reported
	At 1 year post-fracture	11.9		1.5	
	At 2 years post-fracture	18.5%		1.12	
	At 3 years post-fracture	Not reported		1.01	
	At 5 years post-fracture	41.2%		0.92	
	At 10 years post-fracture	75.3%		0.62	
Richmond [43] USA	At 1 year post-fracture	91 (p<0.001)	53	SMR	Not reported
				1.7 (95% CI, 1.3–2.1)	
	At 3 months post-fracture	37 (p<0.001)	13.3	1.7	Not reported
Shah [59] USA	At 1 year post-fracture:		Not reported		Not reported
	<90 years	9.9%		1.48	
	>90 years	26.3%		1.24	
Tsuboi [44] Japan	At 1 year post-fracture	19%		Observed/expected ratio	
				Overall, 2.72	
				<80 years, 5.22	
				≥80 years, 2.15	
				All statistically significant excess versus population norms	
Proportional hazards model (hazard ratios)					
Rapp [19] Germany	Up to 1 year post-fracture				0–3 months
					Women, 1.72 (1.59–1.86)
					Men, 2.14 (1.80–2.53)
Control population was institutionalized elders	At 30 days post-fracture				>3–6 months
	Men	16.1%	7.8%	8.3%	Women, 1.00 (0.89–1.13)
	Women	10.1%	5.3%	4.8%	Men, 1.40 (1.08–1.82)
	At 3 months post-fracture				>6 months–1 year
	Men	34.1%	17.9%	16.2%	Women, 0.81 (0.73–0.91)
	Women	22.8%	14.0%	8.8%	Men, 0.77 (0.58–1.02)
	At 6 months post-fracture				>1 year
	Men	47.5%	30.1%	17.4%	Women, 0.93 (0.87–1.00)
	Women	32.3%	24.3%	8.0%	Men, 1.03 (0.87–1.23)
	At 1 year post-fracture				
	Men	58.3%	48.4%	9.9%	
	Women	44.8%	41.4%	3.4%	
Tosteson [21] USA	Median post-fracture follow-up of 1.5 years	40%	22%	18%	<6 months
					11.6 (8.9–15.1)
					Adjusted for age, sex, and race
					6.28 (4.82–8.20)
					Fully adjusted model[b]
					>6 months
					1.37 (1.16–1.62)
					Adjusted for age, sex, and race
					1.04 (0.88–1.23)
					Fully adjusted model[b]

Table 3 (continued)

Citation (country)	Timeframe	Crude mortality rate		Excess mortality rate	Mortality risk (95% CI)
		Cases	Controls		
Vestergaard [28] Denmark	Not reported			At 1 year post-fracture, 19%	2.26 (2.24–2.27) 1.95 (1.94–1.97) Adjusted for age, sex, and comorbidities Entire follow-up of 20 years
Verstergaard [22][c] Denmark	Actuarial survival at 1 year post-fracture (1996–2001):				
	Overall	28%	5%	24.2%	3.84 (3.77–3.93)
	Men	35%	5%	31.6%	4.78 (4.60–4.96)
	Women	26%	5%	22.1%	3.51 (3.42–3.59)
Wolinsky [24] USA	Up to 8 years of follow-up with risk analysis <6 and >6 months post-fracture	43% (for 8-year follow-up)	38% (for 8-year follow-up)	5% (for 8-year follow-up; p=NS)	Adjusted hazard ratio <6 months, 38.93 (29.58–51.23) >6 months, 1.17 (0.95–1.44)
Relative survival probability calculation					
Giversen [15][d] Denmark	Up to 3 months post-fracture		Not reported		Not reported
	Overall	15.5%		13.6% (12.2–15.0)	
	Men	Not reported		20.4% (17.2–23.6)	
	Women	Not reported		11.2% (9.7–12.7)	
	Up to 1 year post-fracture		Not reported		Not reported
	Overall	26.5%		19.6% (17.7–21.5)	
	Men	Not reported		28.3% (24.2–32.3)	
	Women	Not reported		16.6% (14.5–18.6)	

CI confidence interval, *NS* not significant, *SMR* standardized mortality ratio

[a] Ratio of observed mortality to expected mortality for each age/gender group; >1 indicates excess mortality

[b] Adjusted for age, sex, race, prefracture status, socioeconomic status, facility residence, body mass index, comorbid conditions, and overall health status

[c] Only most recent dataset presented (1996–2001)

[d] Mortality rates estimated using a weighted regression analysis

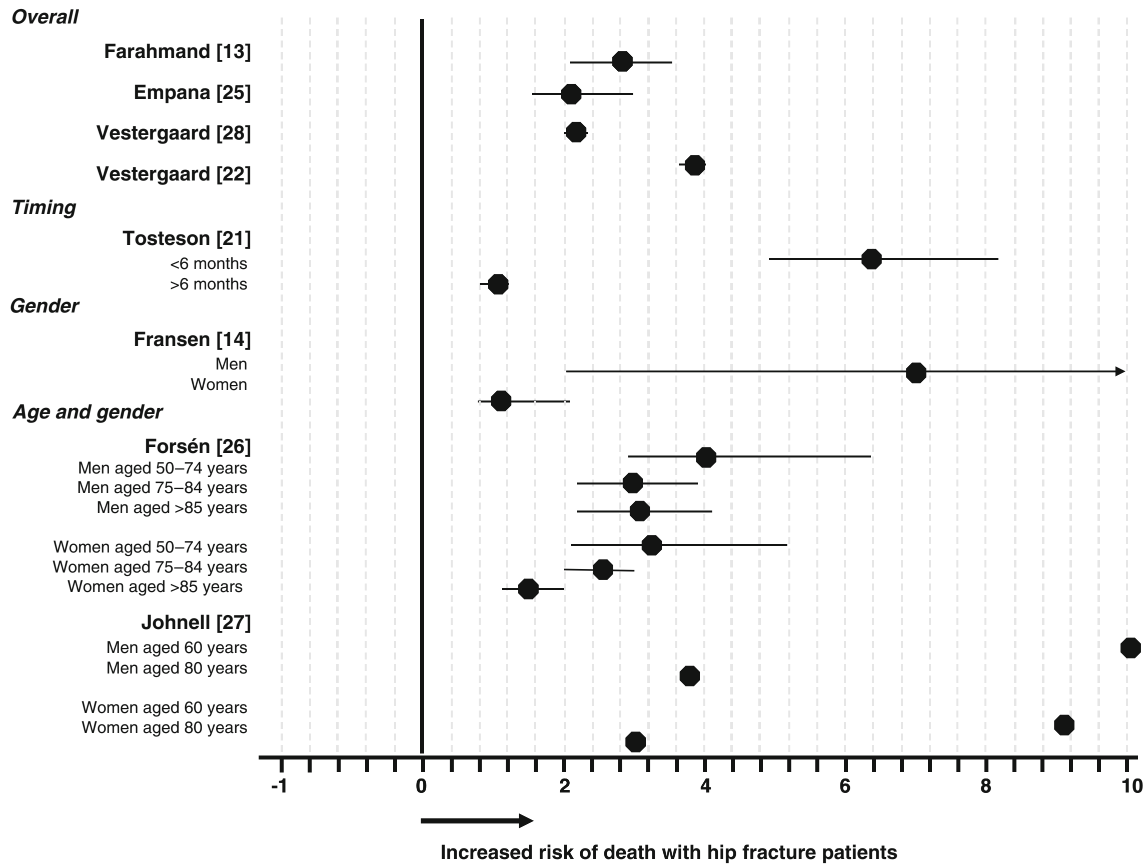

Fig. 1 Forest plot of risk (relative risk, odds ratio, or hazard ratio, with 95% confidence intervals where available) of death following hip fracture compared with general population values

Tosteson and co-workers noted that although mortality rates were higher among men than women in their study, this difference became less pronounced beyond 6 months after fracture [21]. In contrast, Parker and Anand found that among 703 consecutive patients admitted for hip fracture to a single UK hospital, the actuarial mortality rate to 1 year post-fracture was comparable between men and women (37.1% versus 36.6%, respectively) but was considerably in excess of the expected 1-year mortality for age-matched population norms (31.1% and 30.2% excess for men and women, respectively) [17].

Several studies have also revealed a markedly higher mortality rate among men compared with women for up to 20 years after fracture regardless of age [11, 16, 26, 28, 38, 40].

Excess mortality rates compared with age-matched controls

Consistent with the gender specificity of the unadjusted mortality rates, excess mortality compared with age-matched controls was higher among men than women regardless of the measurement employed or age group studied in five studies [11, 15, 19, 22, 27] but similar in one study [17] (Table 3).

Mortality risk and gender

As observed for general inpatient mortality, male patients appear to remain at higher risk of mortality in the months following the index hip fracture, with women having a 38% lower risk of death than men [33]. Three studies have reported that men face at least twice the risk of death following hip fracture compared with women [47, 49, 51]. Holt and co-workers reported an OR for death of 1.93 (95% CI, 1.73–2.14) for men compared with women at 30 days post-fracture [47]. Hindmarsh and co-workers reported an RR of death for men versus women of 2.2 (95% CI, 2.03–2.38) up to 1 year post-fracture [51]. Finally, Boereboom and co-workers found that during a 4-year follow-up, the RR for death was 1.88 (95% CI, 1.40–2.53) for men compared with women [49].

The gender specificity for excess mortality described above was reflected in the higher RR of death compared with the general population for male hip fracture patients than for female hip fracture patients. Forsén and co-workers found that, among patients <75 years old, men were at a 9-fold increased risk and women at a 5-fold increased risk of dying compared with controls during the first 3 months post-fracture [26]. Rapp and co-workers noted that institutionalized male and female elders with hip fracture faced at least twice the risk of death as institutionalized elders without hip fracture, with an increased risk persisting among male residents to 6 months post-fracture [19] (Table 3).

Hip fracture mortality and age

Unadjusted mortality rates

Unadjusted mortality rates following hip fracture increase with age both during the index hospitalization [29, 45, 46, 52] and in the subsequent months and years [13, 17, 20, 25, 28, 31, 35, 36, 40, 41, 49, 51, 53]. One study found that in a cohort of consecutive patients with hip fracture admitted to a single US hospital, separation by general health status negated the effect of age on mortality rates for all except those over 90 years of age [54]. However, data from this study conflict with those reported in the other 13 studies (in which an increase in mortality with increasing age was noted) in that no difference in crude mortality rates was noted for patients <85 years of age compared with those ≥85 years.

Several studies have identified increasing age as a predictor of mortality following hip fracture [16, 18, 22, 32, 33, 41, 48, 50, 55, 56–58].

Excess mortality rates

A number of studies have shown that the excess mortality following hip fracture is highest among younger patients, suggesting that the excess mortality due to hip fracture decreases with increasing age [11, 13, 20, 26–28, 36, 43, 44, 59]. Three studies found that the SMR was higher among younger versus older patients [20, 51, 60].

Mortality risk and age

Bass and co-workers used a Cox proportional hazards model to show that increasing age was positively associated with mortality and that the risk of mortality following hip fracture increased by approximately 5% for each additional year [33].

Two studies conducted risk analyses using younger patients with hip fracture as controls [60, 61]. Both studies found that the RR for death was increased in older compared with younger age groups. In their analysis of data from the Scottish Hip Fracture Audit, Holt and co-workers found that, compared with hip fracture patients aged 50 to 59 years, the OR for death was 1.78 (95% CI, 0.95–0.33) for those aged 60 to 69 years, 3.46 (95% CI, 1.94–6.15) for those aged 70 to 79 years, 5.68 (95% CI, 3.21–10.1) for those aged 80 to 89 years, and 7.11 (95% CI, 3.98–12.7) for those aged 90 years and over [60]. Similarly, Mortimore and co-workers found that among community residents of Baltimore (USA), the RR for death was 1.13 (95% CI, 0.76–1.67) for hip fracture patients aged 75 to 84 years and 1.59 (95% CI, 1.06–2.38) for those aged 85 years and over when compared with those aged 65 to 74 years [61].

Three studies conducted risk analyses compared with general population controls (Fig. 1) [13, 26, 27]. In Norway, the RR was highest among those aged 50–74 years (RR 4.2 in men versus 3.3 in women) in the 12 months after fracture [26]. Similarly, Johnell and co-workers reported that the RR for death following hip fracture in the Swedish population was higher among those aged 60 years than among those aged 80 years [27]. Farahmand and co-workers found that even though the absolute mortality rate increased with increasing age, the RR of mortality following hip fracture compared with general population values decreased from 8.4 among those younger than 70 years to 2.1 among those 76 years or older [13].

Discussion

A systematic review of the literature identified 22 studies that reported excess mortality for patients following hip fracture compared with the general population and a further 41 studies reporting survival data in fracture patients only. The majority of studies have shown that patients with hip fracture experience a significant excess risk for mortality that is at least double that of the age-matched population norms and which persists for several years after the index fracture. Both excess and unadjusted mortality rates among patients with hip fracture indicate that the greatest risk of death is within the first 6 months after the index fracture. In addition, most studies have confirmed that mortality following hip fracture increases with increasing age, although the excess mortality versus age-matched population norms decreases with increasing age. In other words, while older patients have higher mortality following hip fracture in absolute terms, the RR of death is greater in younger age groups where the expected risk of all-cause death is lower. Finally, in general, men face a greater excess risk of death after fracture than women regardless of the measurement employed or age group studied.

To our knowledge, the results reported here represent the first systematic analysis of the evidence base for excess mortality associated with hip fracture. However, there was a lack of consistency in the study designs and the statistical analyses used to determine excess mortality across the 22 studies that reported such data. Consequently, no meta-analysis or pooled analysis of the current dataset was possible.

The extent to which underlying conditions contribute to the excess mortality associated with hip fracture is unclear. Numerous studies have reported that the presence of concomitant medical illness or poor health status are negative predictors for survival following a hip fracture [16, 18, 20, 28, 31–33, 36, 37, 42, 43, 45, 49, 52, 54, 56, 57, 60, 62, 63], while other studies have found no association between concurrent life-threatening disease and mortality after hip fracture [50] nor an increased risk of death regardless of the presence of comorbid illness [13]. Tosteson and co-workers found that while adjustment for a variety of factors, including prefracture functional status and comorbid conditions, did not fully account for the excess mortality observed in the first 6 months after fracture, adjustment for these factors did eliminate the observed excess mortality beyond 6 months post-fracture [21]. Kanis and colleagues noted that hip fracture per se (rather than comorbidities) accounted for 17–32% of deaths in patients with hip fracture and was responsible for 1.5% of all deaths among persons aged 50 years or older [11]. In a separate large cohort study, Vestergaard and colleagues demonstrated that post-fracture conditions related to the trauma experienced had a greater influence on mortality than prefracture comorbidities [28]. Trauma-related complications accounted for 70.8% of the deaths occurring within 30 days of hip fracture, decreasing to 7.6% of deaths occurring more than 30 days after the fracture [28]. It is possible that the high proportion of in-hospital deaths classified as trauma-related on death certificates in this study may reflect the requirement to classify deaths in this way if there is any doubt that the death is due to natural causes. Accordingly, several studies have highlighted the contribution of selected comorbidities that increase or at least contribute to the higher risk of death following hip fracture including metastatic cancer, congestive heart failure, renal failure, liver disease, lymphoma, infection, and weight loss [13, 33, 45, 52, 64].

There are few data that can help determine whether hip fracture-related mortality has increased or decreased in recent years. Available studies have provided conflicting results: two studies suggest a trend toward increasing mortality following hip fracture in recent years [22, 65], while two other studies failed to identify either an increase or a decrease in hip fracture-related mortality in recent years [39, 66]. However, even with a stable rate of death following hip fracture, the actual number of fractures can be expected to increase in line with a growing and increasingly elderly global population.

Most patients presenting with hip fracture are treated surgically. Possible causes of death following surgical intervention for hip fracture include cardiac and pulmonary complications, infections (such as pneumonia, influenza, and septicemia), and an increased risk of thromboembolism [35, 37, 67]. A recent report indicated that 39% of inpatient deaths among patients with isolated limb and pelvic fractures were due to bronchopneumonia [35]. Lawrence and colleagues found that the risk of mortality increased with the number of postoperative complications and that serious cardiac and pulmonary complications were the most significant with respect to risk of death [37]. The relationship between the timing of surgery and the subsequent mortality risk has been the subject of some debate. There is evidence to suggest that patients who undergo hip fracture stabilization surgery within 48 h of the fracture event are at a reduced risk of death compared with those whose surgery is delayed [68–70]. However, there may be a number of barriers to achieving such early surgery including the patient's health status. Two studies found an increased risk of death, including death due to infection, among patients whose surgery was delayed beyond 72 h after admission [71, 72] but other studies have failed to find any significant benefit of early surgery (<24 h post-fracture) in terms of subsequent mortality [73, 74]. Furthermore, two studies found that for otherwise medically fit individuals, a delay of at least 4 days after admission did not appreciably affect survival [75, 76]. Surgery within 48 h of hospital admission may be difficult to achieve due to both organizational reasons and patient factors such as health status at the time of fracture [68]. While it has not yet been definitively demonstrated that early (<48 h after admission) treatment reduces the subsequent risk of mortality, it is widely regarded as prudent to surgically stabilize the fractured joint as soon as possible. The Royal College of Physicians guidelines recommend surgical repair within 24 h of admission [68].

Possible reasons for the increased mortality risk faced by men versus women following hip fracture are still poorly understood. One study suggested that a gender difference in terms of infection rates (notably pneumonia and septicemia) may contribute to the differential risk [77], although the etiological reasons for this remain unclear. In two studies, men were more likely to have a higher American Surgical Association (ASA) rating of operative risk (a system that assesses patients in terms of general disease burden [78]) than women, suggesting that men had more severe medical comorbidities prior to the index hip fracture [30, 47]. Endo and colleagues also reported that male gender was associated with an increased risk of postoperative complications, including pneumonia, arrhythmia, delirium, and pulmonary embolism, even after controlling for age and ASA rating [30]; other studies have failed to demonstrate such a link [79].

Patients experiencing one fragility-related hip fracture are at increased risk for subsequent fractures [80–83].

Despite this, it would appear that such patients are inadequately investigated [82] and often do not receive the recommended or adequate treatment [8–10, 84]. Notably, few patients who have experienced a hip fracture are prescribed osteoporotic treatments such as bisphosphonates, and in many cases only calcium and vitamin D are prescribed. Treatment rates of around 20–30% are generally cited [85–90] but estimated treatment rates vary considerably, possibly reflecting local practices in different countries [85–90]. Encouragingly, recent studies have indicated that pharmacologic treatment for osteoporosis may decrease the risk of subsequent hip fractures [91] and potentially also the increased risk of death [92]. Non-pharmacological approaches to maximizing peak bone mass, such as regular exercise and calcium and vitamin D supplementation, are established approaches to the management of osteoporosis and may also contribute to the prevention of fractures [93]. Indeed, there is some suggestion that interventions such as nutritional supplementation [94] and dietetic assessment [95], comprehensive multidisciplinary intervention programs [96, 97], and in-hospital rehabilitation programs [98] may also improve outcomes, including mortality.

By conducting a systematic review of the current evidence base with regard to hip fracture-related mortality, we have confirmed the assumption that patients with hip fracture experience a marked and significant excess risk of death.

Despite calls to improve the identification, assessment, and treatment of patients at risk of first or subsequent osteoporotic hip fractures [10, 87], many patients remain poorly treated on discharge from hospital [8, 9]. Our review has raised a number of questions, perhaps the most important of which is why there has been an apparent increase in mortality following hip fracture. Additional research is now needed to identify the reasons for the apparent increase in post-hip fracture mortality and to develop methods to distinguish between health outcomes that are a direct consequence of the fracture and those that result from pre-existing/comorbid medical conditions. Future research should also focus on establishing whether and which interventions, such as those for osteoporosis, can effectively reduce the risk of death following hip fracture. Properly viewed, the high and long-lasting excess mortality risk associated with hip fracture should be a strong incentive rather than a barrier for the establishment of tertiary prevention programs for osteoporotic fractures, including fracture liaison services. There is a need to ensure evaluation for osteoporosis in all patients following hip fracture and to implement and ensure long-term compliance with treatment regimens, including pharmacotherapy, with demonstrated improvement in treatment outcomes and adherence to therapy.

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