Variation in Risk Factors for Fractures at Different Sites

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Fractures in older people are important medical problems. Knowledge of risk factors is essential for successful preventive measures, but when fracture sites of diverse etiology are combined, risk factors for any one site are difficult to identify and may be missed entirely. Among older people, incidence rates of hip, proximal humerus, and vertebral fractures increase with age, but not rates of distal forearm and foot fractures. Low bone mineral density is strongly associated with hip, distal forearm, vertebral, and proximal humerus fractures, but not foot fracture. Most fractures of the hip, distal forearm, and proximal humerus result from a fall, whereas smaller proportions of fractures of the foot and vertebrae follow a fall. Frail people are likely to fracture their hip or proximal humerus, while healthy, active people tend to fracture their distal forearm. We strongly recommend that studies identify risk factors on a site-specific basis.

Introduction

Fractures in older people are common, disabling, and costly. Burge et al. [1•] estimated that in 2005 more than two million incident fractures occurred among people of age 50 years and older in the United States, at a cost of $17 billion. With the increasing number of older people in the population, the estimated number and costs of fractures are expected to rise by almost 50% by 2025. Thus, prevention of fractures, already important, will become even more so over the next few decades.

Knowledge of risk factors is essential for successful preventive efforts. As early as 1959, Buhr and Cooke [2] pointed out that based on only such readily accessible characteristics as age and sex, fracture incidence rates differ considerably by fracture site. More recently, Seeley et al. [3] and then Stone et al. [4], using data from the Study of Osteoporotic Fractures, have shown that although among women age 65 years and older fractures of most sites are associated with low bone mineral density, the strength of the association varies considerably from one fracture site to another (Table 1). Such common sites as the foot, ankle, and toe, for instance, have only weak associations with bone mineral density. Furthermore, the associations with age vary considerably (Table 2). Although fractures of the hip, humerus, and pelvis show steep increases in the older age groups, the other sites do not.

Despite these variations in basic features of the epidemiology of fractures of different sites, many epidemiologic studies of osteoporotic fractures combine fractures of all sites, or of all sites except the hip and vertebrae. When conditions of different etiology are combined, associations with individual entities can be so diluted that they are completely missed or considered unimportant.

This article discusses similarities and differences in risk factors for common fracture sites in older individuals. As examples we focus on five sites: hip, distal forearm, vertebrae, proximal humerus, and foot.

Hip Fracture

Risk factors for hip fracture have been studied to a much greater extent than fractures of any other site. Hip fractures are common in the elderly, and are associated with increased mortality, high costs, and substantial disability. Table 2 shows that incidence rates among women in the Study of Osteoporotic Fractures increased exponentially from 1.4 per 1000 person-years in the age group 65 to 69 years to 10.7 per 1000 person-years in the age group 80 years and older. Within the United States and other Western countries, at a given age incidence rates are about twice as high in women as in men. Recent data indicate a decrease in hip fracture incidence over the decade 1996 to 2006 [5].

Low bone mineral density is relatively strongly related to risk for hip fracture (Table 1) [3,4,6,7•], more so in the decades around age 60 years than around age 80 years [6]. Risk factors include a history of falls, a maternal history of hip fracture, a personal history of fracture, low body

Table 1. Age-adjusted hazard ratios (and 95% CIs) for the associations of BMD in the spine and hip with fracture sites with $N \geq 100$ over 8.5 years of follow-up in nonblack women 65 years of age and older in the Study of Osteoporotic Fractures

Fracture site	Number of fractures	BMD, total spine (hazard ratio* [95% CI])	BMD, total hip (hazard ratio* [95% CI])
Any fracture	2044	1.33 (1.27–1.40)	1.46 (1.39–1.53)
Hip	474	1.49 (1.34–1.65)	2.22 (2.00–2.47)
Distal forearm	438	1.62 (1.46–1.81)	1.67 (1.50–1.86)
Spine	361	2.06 (1.80–2.35)	2.01 (1.77–2.28)
Humerus	280	1.78 (1.55–2.05)	1.99 (1.74–2.28)
Rib	229	1.42 (1.23–1.64)	1.63 (1.41–1.89)
Foot	210	1.20 (1.04–1.39)	1.22 (1.05–1.42)
Ankle	193	1.10 (0.95–1.27)	1.07 (0.92–1.25)
Pelvis	121	1.74 (1.41–2.15)	2.05 (1.66–2.52)
Toe	107	1.28 (1.04–1.58)	1.24 (1.01–1.53)

*Hazard ratio associated with a 1-SD increase in BMD. An SD at the total spine is 0.17 g/cm^2 and at the total hip is 0.13 g/cm^2.
BMD—bone mineral density; CI—confidence interval.
(*Data adapted from* Stone et al. [4].)

Table 2. Incidence rates per 1000 woman-years in nonblack women 65 years of age and older, by fracture site and age group, in the Study of Osteoporotic Fractures

Fracture site	Age group			
	65–69 y	70–74 y	75–79 y	≥ 80 y
Hip	1.4	3.2	6.4	10.7
Distal forearm	8.1	8.3	9.7	9.4
Humerus	2.7	4.5	3.6	7.1
Ankle	3.9	4.4	3.3	4.9
Foot	4.9	4.1	5.3	4.0
Rib	2.2	3.5	4.5	3.2
Patella	1.1	0.9	1.7	3.1
Pelvis	0.4	1.2	2.5	2.7
Toe	3.9	2.0	2.8	1.8

(*Data adapted from* Seeley et al. [3].)

weight, weight loss, greater height, poor self-rated health, a relatively low level of physical activity, various medical conditions such as certain endocrine disorders, Parkinson's disease, and type 2 diabetes mellitus, medications such as corticosteroids, long-acting benzodiazepines, and anticonvulsant drugs, high plasma homocysteine concentration, neuromuscular impairments as indicated by inability to rise from a chair, slow walking speed, lower limb dysfunction, and low muscle strength, visual deficiencies, low resting pulse rate, depression, dementia, and cigarette smoking. Menopausal hormone therapy is protective. Weaker or less consistent positive associations have been found with increased caffeine intake and low calcium and vitamin D intake, while some evidence suggests that thiazide diuretic use may be protective [8•,9–12].

Long hip axis length is associated with a higher risk. Other indices of femoral geometry, including femoral neck diameter, cross-sectional moment of inertia, and section modulus, and microarchitectural characteristics, including trabecular connectivity and spacing as estimated by quantitative ultrasound, probably also affect risk independently of bone mineral density [13].

The immediate cause of most hip fractures is a fall [14]. Cummings and Nevitt [14] proposed that persons who have difficulties with gait and balance are more likely to fall in a position that results in impact on the hip, and that those with less muscle strength and slower reaction time may be less able to break a fall with an outstretched arm. Falling straight down or in a lateral direction in which one lands on the hip is especially likely to result in a hip fracture [15–17]. Breaking the fall with an outstretched hand or knee and falling forward or backwards are associated with a lower risk compared with falls in other directions [16,17]. Falling from a greater height and landing on a hard surface increase the risk [16]. The association of low body mass index with hip fracture is probably attributable in part to the greater padding over the hip in persons with higher body mass index, so that the stress on the bone is less when the hip is the point of impact.

Thus, hip fracture tends to occur among frail individuals who are at increased risk for falling and less likely to be able to protect themselves in the event of a fall by breaking their fall, and more likely to have poor quality bone. Measures to prevent loss of bone mass, to prevent falls, and to improve overall health should reduce the risk for hip fracture.

Distal Forearm Fracture

Fracture of the distal forearm (radius or ulna) is the most common fracture among white women under 75 years of

age in the United States and northern Europe. Although less disabling than fractures of many other sites, distal forearm fractures can be associated with pain and limitations in multiple activities of daily living [18]. In the United States, incidence rates in women increase from age 45 to 65 years, but are relatively level thereafter. In men, rates are relatively stable after 45 years of age [19]. Overall, age-adjusted incidence rates are about four times higher in women than men, with the female excess greater at older than at younger adult ages.

Low bone mineral density is known to increase the risk for distal forearm fracture [3,4,20]; a history of fractures since age 45 to 50 years, probably a rough marker of osteoporosis, is also associated with an increased risk [21–23]. Recent use of menopausal hormone therapy is protective [24,25]. Some studies have reported that other factors known or postulated to protect against loss of bone mineral density, such as thiazide diuretic use [21,26], high dietary calcium intake [21,27], and higher body mass index, especially in women [21,27] are associated with a lower risk. However, other studies do not find any association with calcium intake [28,29], and body mass index may not have an independent effect once bone mineral density is taken into account [13].

More than 90% of distal forearm fractures occur as a result of a fall [20,21,30]. Falling from greater than a standing height, falling backwards or obliquely forward, landing on the hand, and putting out the hand to break a fall are associated with increased risk [16,30,31]. One study found that activities associated with highest risk were reaching up, vigorous exercise, and other outside activities [31].

A history of falls is associated with a somewhat elevated risk [20,22,26]. Risks for distal forearm fracture according to attributes generally associated with an increased risk for falling and that would be expected to be related to increased risk for distal forearm fracture have been less well studied. However, in a few studies, increased risks have been associated with use of seizure medication and a history of epilepsy [21,23], a history of depression [21], fall-related medical conditions [23], poor vision [20], and winter and freezing temperatures [32]; however, another study did not find poor vision to be associated with increased risk [26].

In contrast to hip fracture, distal forearm fractures do not tend to occur in frail individuals [20,21,26–28,33]. In fact, brisk [28] and frequent [20] walking have been associated with an increased risk and lack of physical activity [20,26,28,33], impaired walking ability [33], and going outdoors infrequently [33] with a decreased risk Moreover, foot problems [34], diabetes mellitus [23], and lower extremity problems in general [21] are associated with a decreased risk for distal forearm fracture, suggesting that attributes that cause people to move more slowly decrease risk.

Thus, distal forearm fractures tend to occur as a result of a fall on an outstretched hand in persons with low bone mineral density who are otherwise in relatively good health. Persons in poorer health and with slowed reflexes tend to move slowly and are unable to put out their hand to break a fall, and in so doing, decrease their risk for distal forearm fracture (and perhaps increase their risk for fractures at other sites such as the hip and proximal humerus).

Vertebral Fracture

Vertebral fractures, many of which are not clinically diagnosed, are the most common osteoporotic fracture, affecting as many as half of white women and men in their 80s in the United States [35,36]. These fractures occur most commonly in the mid-thoracic region (T7-T8) and thoracolumbar junction (T12-L1) in both women and men, but the reasons for this distribution are unknown. Vertebral fractures cause pain, disfigurement, depression, and functional impairment [37,38]. Moreover, vertebral fractures may be harbingers of future disabling fractures of several sites as well as of death [39•,40]. Despite the impact of vertebral fracture, less than one third of individuals with vertebral fractures receive medical attention and even fewer are treated [41]. Further, because diagnosis of incident vertebral fracture requires at least two radiographic assessments at appropriate intervals and because only a minority of cases are clinically recognized, identifying risk factors for vertebral fracture is particularly challenging compared with other major fracture sites.

The prevalence of vertebral fracture is similar in women and men in middle-age years, but the incidence rate is two to three times greater in women than men in later years [42•], suggesting that trauma or factors other than osteoporosis may play a significant etiologic role in vertebral fracture in men and younger women. Although older age and low bone mineral density are known to increase the risk for vertebral fracture, the strongest predictor of a future vertebral fracture in women and men is an existing vertebral fracture [39•,42•,43]. Nonvertebral fractures are also associated with increased incidence of subsequent vertebral fracture [43,44].

Population-based prospective studies, including Framingham [42•], Rotterdam [43], and the European Prospective Osteoporosis Study [45], have shown weak or no associations between body weight, height, and physical activity and incident vertebral fracture in women or men. The Study of Osteoporotic Fractures [44], in contrast, reported low body mass index and low physical activity to be associated with an increased risk of first vertebral fracture in women. Results for smoking [43,44] and alcohol consumption [42•] are also mixed, with some reporting increased vertebral fracture incidence and others finding no association [42•,45]. Women with hyperthyroidism who are not treated or inadequately treated have been reported to be at increased risk for vertebral fracture [46]. Use of menopausal hormone therapy among women has been shown to be protective [44,45]. Little is known of the role of frailty as a risk factor for vertebral fracture.

Some evidence indicates that a history of falls is associated with an increased risk of vertebral fracture [44], but the role of falls in the etiology of vertebral fracture is largely unknown. In a population-based cohort study in Rochester, Minnesota, Cooper et al. [47] found that falls precede 30% of vertebral fractures. Everyday activities, such as lifting, doing housework, and opening a window can lead to vertebral fracture. From a review of charts of patients with acute vertebral fractures, Patel et al. [48] found that half the patients reported that the fractures occurred "spontaneously."

In summary, similar to some other osteoporosis fractures, vertebral fractures are associated with increasing age, low bone mineral density, and female gender, but other risk factors associated with low bone mineral density, such as low body mass index, smoking, and low physical activity level, are weakly related or unrelated to these fractures. The role of falls and activities leading to vertebral fractures are poorly understood. Learning more about the pathophysiologic and biomechanical mechanisms involved in vertebral fracture etiology is of high priority.

Proximal Humerus Fracture

Fracture of the proximal humerus is the second most common fracture of the upper extremities, following distal forearm fracture, and accounts for 10% of all fractures in people age 65 years and older [49]. Incidence rates rise steeply in women after around age 45 to 50 years; rates rise in men as well, but somewhat more gradually. Women have two to three times the risk of proximal humerus fracture as men.

Relatively few studies have been undertaken to identify risk factors for proximal humerus fracture. Low bone mineral density is known to increase the risk for proximal humerus fracture [3,4,20,50]. Factors associated with low bone mineral density, including height loss since age 25 years, a history of previous fractures, a low level of physical activity, impaired balance, and pain in the lower extremities, have been associated with an increased risk [20,50,51]. Results have been inconsistent as to whether a low body mass index and low dietary or supplemental calcium intake are associated with an increased risk Menopausal hormone therapy has been found to be protective, especially if use has been recent [20,25].

Some 90% to 97% of proximal humerus fractures result from a fall [30,51]. Falling obliquely forward or sideways, falling from more than a standing height, and landing on a hard surface, and especially landing on the shoulder have been reported to be associated with elevated risk [30,31]. Using walking as the reference activity, one study found that the activities most often associated with a fall that led to a fracture were turning around and performing a vigorous activity, while descending stairs was associated with a lower risk than walking [31].

A history of falls and risk factors for falls have been associated with proximal humerus fracture [20,50,51]. Risk factors for falls that also appear to be risk factors for proximal humerus fracture include some indicators of poor vision, diabetes mellitus, various indicators of neuromuscular impairment, epilepsy and/or seizure medication use, depression, use of a hearing aid, and left-handedness [20,50,51].

Two cohort studies indicate that people who fracture their proximal humerus tend to be less active and more frail than average [20,50]. Some studies suggest that self-reported poor health and poor neuromuscular function are associated with increased risk [20,50]. It has been hypothesized that, as with hip fracture, frail people are more likely to fall and, in the course of a fall, are less likely to put out a hand quickly enough to break the fall [20].

In summary, persons at high risk for proximal humerus fracture generally have low bone mineral density and a tendency to fall. They also tend to be frail, but the association with frailty does not appear to be as strong as for hip fracture [51].

Foot Fracture

Foot fractures are one of the most common fractures among older persons, and are associated with large decreases in physical and social functioning. Nevertheless, only limited study of risk factors has been undertaken. Women are affected about twice as frequently as men, and incidence rates do not increase with age in adults [3,52].

Foot fracture is only weakly associated with low bone mineral density [3,4]. Risk factors include type 2 diabetes, insulin-dependent diabetes, use of benzodiazepines and seizure medications, a history of falls, prior fractures, visual problems, and foot problems [52–55]. Factors generally considered protective against osteoporotic fractures, including use of menopausal hormone therapy, thiazide diuretics, high calcium intake, and high body mass index, do not appear to be associated with risk for foot fracture. Greater physical activity has been associated with a reduced risk for foot fracture [52,55].

About 60% of foot fractures are attributable to falls, and about 20% to non-fall trauma [52,54]. Thus, falls are somewhat less important than for most other appendicular fracture sites. The falls tend to result from hitting the foot or misstepping, particularly on sidewalk curbs and while descending stairs, and the non-fall trauma from twisting or turning a foot [31,52,54].

In summary, risk factors for foot fracture in older people identified to date are mainly characteristics that reduce visual acuity and mobility and increase loss of feeling in the foot. In general, factors associated with increased bone mineral density do not protect against foot fracture. Efforts to control diabetes and maintain vision and mobility, along with greater caution around curbs

Table 3. Direction and strength of associations between selected characteristics and fractures of the hip, distal forearm, spine, proximal humerus, and foot in women 65 years of age and older

Characteristic	Fracture site				
	Hip	Distal forearm	Vertebrae	Proximal humerus	Foot
Increasing age	Steep increase	No increase	Moderate-steep increase	Steep increase	No increase
Low bone mineral density	Strong	Strong	Strong	Strong	Weak
Percentage of fractures attributable to a fall	> 90%	> 90%	25% to 60%	> 90%	60%
Frailty	Strongly positive	Negative	Uncertain	Moderately positive	No association
Most frequent direction(s) or mechanism of fall	Straight down or lateral, landing on hip	Backwards or obliquely forward, putting out hand to break fall	Uncertain	Forward, sideways, or landing on shoulder	Hitting the foot or misstepping

and when descending stairs, should reduce the frequency of foot fractures [52].

Conclusions

Risk factors vary for fractures of these five sites (Table 3). The incidence rates of hip and proximal humerus fractures increase markedly with age; vertebral fracture shows some increase in incidence with age, whereas distal forearm and foot fractures show no increase in incidence with age in older people. Low bone mineral density and risk factors for low bone mineral density are associated with fractures of the hip, distal forearm, vertebrae, and proximal humerus, but low bone mineral density is only weakly associated with foot fracture. The vast majority of fractures of the hip, distal forearm, and proximal humerus result from a fall, whereas a smaller proportion of fractures of the vertebrae and foot are caused by a fall. The direction of the fall and ability to break a fall with an outstretched hand are major determinants of fracture site. Frail people, who are generally unable to break a fall, tend to fracture their hip or proximal humerus, while healthy, active people are better able to break their fall with an outstretched hand, but in so doing may fracture their distal forearm. In addition, therapeutic trials show different effects of therapeutic agents on fractures of different sites. For instance, for reasons that are unclear, raloxifene protects against vertebral but not hip fracture [56].

The risk factors for hip and proximal humerus fractures show some similarities, but the other three fracture sites have distinctly different patterns. When the fracture sites are combined, the risk factors for any one site may be difficult to identify, and the strengths of associations seriously diluted. Therefore, we strongly recommend that studies identify risk factors on a site-specific basis.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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