Epidemiology of Hip Fractures

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Hip fractures are the most serious osteoporotic fracture at both an individual and population level. In the United States alone there are over 250,000 hip fractures each year (1), costing at least 5.4 billion dollars annually (2). About 20 percent of persons who fracture their hip are dead within a year (3, 4) and, of the survivors, many never regain their prefracture level of physical function (5, 6).

INCIDENCE OF HIP FRACTURES

Cooper et al. (7) estimated that about 1.7 million hip fractures occurred worldwide in 1992. The incidence of hip fracture rises dramatically with increasing age (figure 1). Jacobsen et al. (8) estimated that, in the mid-1980s in the United States, the annual incidence in 65-year-old white women was 1.6 per 1,000 compared with 35.4 per 1,000 in 95-year-old white women. The incidence of hip fracture is higher in women than in men. In the study by Jacobsen et al. (8), the age-adjusted hip fracture incidence rates in white US males and females were 4.3 and 8.1 per 1,000 per year, respectively (8). A white woman has a 16 percent lifetime risk of suffering a hip fracture, and a white man has a 5 percent lifetime risk (9).

Hip fracture incidence according to race and geography

Variation in hip fracture incidence rates according to geographic area and race/ethnicity has recently been reviewed by Maggi et al. (10) and by Villa and Nelson (11). The highest age-adjusted hip fracture incidence rates (generally >6 per 1,000 per year) have been reported among predominantly white populations in Norway, Sweden, Denmark, the United States, and Canada. Age-adjusted incidence rates of around 4–6 per 1,000 per year have been reported from Finland, England, Scotland, and New Zealand, and rates of around 2–4 per 1,000 per year have been observed for Asian populations in recent studies in Hong Kong, Japan, and the United States and in black and Hispanic populations in the United States. The lowest incidence rates were from Singapore, Hong Kong, and South Africa in the 1950s and 1960s, although rates in Hong Kong have increased substantially since that time (12).

In countries in which incidence rates are high, the female-to-male ratio of age-adjusted incidence rates is generally around 2:1 or greater. This ratio tends to decrease as incidence rates become lower and, in the early studies in Singapore and South Africa, was close to 1:1. Within the United States, a study in California (13) found age-adjusted incidence rates of 6.2 per 1,000 among white females, 3.8 per 1,000 among Asian females, 2.4 per 1,000 among black females, and 2.2 per 1,000 among Hispanic females. In all but blacks, the ratio of female-to-male incidence rates was greater than 2:1.

Methodological variation from one study to another may explain some, but not all, of the apparent differences from one geographic area to another. Among the sources of variation are differences in how hip fractures are defined, in the way hip fractures are coded, in the case ascertainment methods used, and in the extent to which readmissions for the one fracture are eliminated.

Higher bone mass may contribute to the low incidence rates in blacks (14) and Hispanics (15), but bone mass among Asians is similar to that in whites (16). Shorter hip axis lengths in Asians, blacks, and Hispanics than in whites have been reported (17, 18); this may be one reason for their lower hip fracture rates. Also, traditional measurements of bone mineral density do not take into account bone volume, and the smaller bone volume in Asians than in whites needs to be considered when interpreting the relation between bone mineral density and fracture risk (19). Other hypothesized reasons for the variation in incidence rates by geography and race/ethnicity include differ-
Changes in hip fracture incidence over time

Increases in crude hip fracture incidence rates during the 20th century have been observed in many developed countries. Much of the increase in crude incidence rates can be attributed to simple population aging, but there is also evidence from several countries of an increase in the age-specific incidence rate of hip fracture. For example, crude rates of hip fracture in Rochester, Minnesota, increased by 178 percent between 1940 and 1980, while age-standardized rates increased by 53 percent (20).

There is convincing evidence of secular increases in hip fracture risk among men in northwestern Europe and North America, but the evidence for women in these same regions is conflicting. Nearly all studies from Scandinavian countries (20–27), the United Kingdom (20, 28), and North America (20, 29–31) have found 1–4 percent annual increases in hip fracture incidence rates in men after adjusting for age. In women, however, most of these same studies found no increase in incidence rates over time. There is some evidence that incidence rates in women may have increased in earlier decades of this century but have stabilized more recently (20, 28). For example, in Rochester, a large increase in age-standardized rates of hip fracture among women was observed between 1940 and 1955, but there was no change from 1955 to the late 1980s (20). It is uncertain whether the conflicting findings for women reflect methodological problems, such as incomplete age-standardization, or real geographic differences.

Trends over time in diet, cigarette smoking, and alcohol use have been proposed to explain the observed secular trends (20, 21). Another hypothesized factor is an increasingly sedentary life-style in advanced industrial societies, especially among men.

RISK FACTORS FOR HIP FRACTURES

The high rate of hip fracture in older people has two main causes: increased skeletal fragility and increased risk of fall-related trauma. Most risk factors for hip fracture probably involve one, or both, of these pathways.

Skeletal fragility

Bone strength is strongly related to bone mass, with correlation coefficients from 0.6 to 0.8 between bone mineral density and the force required to fracture a bone (32). Bone strength is also a function of its geometry, microarchitectural integrity, and other qualitative parameters. The length of the proximal femur (33) and its cross-sectional area (34) may influence its strength. Thinning and increased porosity reduce the strength of cortical bone, while thinning, perforation, and loss of connectivity in the trabecular plates weakens the internal supporting structure of vertebrae, the distal radius, the proximal femur, and flat bones such as the ribs (35).

Prospective studies of bone mineral density measurement for prediction of hip fracture have recently been reviewed by Marshall et al. (36). Using meta-analytic techniques to combine the findings of several studies, they concluded that a one standard deviation decrease in bone mineral density at the hip is associated with a relative risk for hip fracture of 2.6. The equivalent relative risks for hip fracture were 1.4 for bone mineral density in the forearm and 1.8 for vertebral bone mineral density.

Ultrasound is a promising tool for assessing bone quality. The speed at which sound travels through bone probably depends on both bone mass and the micro-architecture of the bone. For example, multiple trabecular micro-fractures would be expected to reduce the speed of sound through bone. Ultrasound has been used as a tool to measure bone quality at the calcaneus and patella, and its use at other sites, such as the tibia, is being investigated. Several studies have found that ultrasound characteristics (broadband attenuation and speed) are associated with risk of hip fracture (37–41). In the largest of these studies, a one standard deviation decrease in broadband ultrasound attenuation measured in the calcaneus was associated with a relative risk for hip fracture of 2.0 (40).

Although assessment of bone mass from radiographs has long been replaced by bone absorptiometry techniques, Gluer et al. (42) recently published evi-
dence that radiographs of the proximal femur could still be useful for predicting hip fractures. They showed that hip fractures were associated with reduced thickness of the cortexes of the femoral shaft and femoral neck, wider trochanteric region, and poor macroscopic trabecular structure. The work of Glaer et al. (42) extended the original observations by Singh et al. (43) that radiographic trabecular patterns were associated with osteoporotic fractures.

In the last few years, investigators have started to study the relation between some geometric characteristics of the femur and risk of hip fracture. For example, Faulkner et al. (33) used bone densitometry scans to measure the distance from the greater trochanter to the inner pelvic brim (called hip axis length), the angle between the femoral neck and the shaft of the femur, and the width of the femoral neck. Hip axis length was longer in women who subsequently fractured their hips than in those who did not. This finding has been confirmed by others (44).

FALL-RELATED TRAUMA

About 90 percent of hip fractures are associated with a fall, with the vast majority of such falls being from a standing height or less (45). Cohort studies have found that people who fell at least once in the year prior to baseline interview had about a 50 percent greater risk of subsequent hip fracture than people who had not fallen (46, 47).

Although falls are frequent among older people, only 1–2 percent of falls lead to hip fractures (45). It has been hypothesized that for a fall to result in a hip fracture, the faller must be oriented so that the point of impact is on or near the hip and that protective responses (such as landing on an outstretched hand) and shock absorbers (such as soft tissue over the hip) fail to reduce the energy to a level less than that required to break the proximal femur (figure 2) (48). Aspects of this hypothesis have been tested epidemiologically and biomechanically.

Biomechanics is the application of engineering mechanics to biologic systems, and represents a useful complement to epidemiologic studies of hip fracture. Biomechanical studies support the notion that a direct fall on the hip creates a high risk of hip fracture, since both the energy available in a fall from a standing height and the force generated during impact on the hip are far greater than required to fracture an older person’s femur (49–51). There is evidence that younger femurs (mean age 33 years) can absorb twice the force and three times the energy of older femurs (mean age 74 years) before fracturing (52), perhaps explaining in part why young people are unlikely to suffer fall-related hip fractures.

Recent case-control studies have compared characteristics of falls that caused hip fractures with the characteristics of falls that did not (53–55). These studies have shown that the risk of hip fracture in fallers is increased in falls from greater than a standing height, in sideways falls and falls directly onto the hip, in falls with weak or absent protective arm responses and falls on to hard surfaces, and in fallers with less soft tissue.

Laboratory testing of hip pad devices under simulated falling conditions have demonstrated attenuation in impact forces by up to 65 percent (56). The effectiveness of such devices has been demonstrated in a randomized trial in Danish nursing homes (57). The intervention group had half the hip fracture rate of controls despite incomplete compliance in the intervention group. Another promising engineering-based strategy for fracture prevention is increasing the energy-absorbing capacity of floor surfaces in high risk environments such as nursing homes (58).
GENETICS AND FAMILY HISTORY

Studies of twins and mother-daughter pairs have shown that much of bone mass is genetically determined (59). It was recently reported (60) that variants of the vitamin D receptor gene were associated with large differences in bone mass. Although this finding has not been confirmed by all subsequent studies (61, 62), it has generated enormous interest in the molecular genetics of osteoporosis. There has, however, been little research to date on the importance of family history of osteoporosis and fractures in hip fracture etiology. The only relevant study (46) found that women who reported that their mothers had had a hip fracture had twice the risk of hip fracture of women without this family history.

HORMONAL FACTORS

Reproductive hormones are important in the establishment and maintenance of peak bone mass at early ages and affect the rate of loss of bone mass in the postmenopausal years (63). Most evidence suggests that estrogen acts primarily to reduce bone resorption.

Hormone replacement therapy

Randomized trials have clearly established that replacement estrogen prevents or greatly retards loss of bone mass in both oophorectomized women and in women with intact ovaries (64, 65). When estrogen administration ceases, loss of bone mass continues, although whether it is at the same rate as in women of similar age who have never used estrogen (65), or at the accelerated rate that occurs just after menopause (64, 66) is uncertain. A dose of 0.625 mg per day of conjugated estrogen is sufficient for protection (67). The beneficial effect of estrogen does not vary with route of administration (oral, transdermal, percutaneous, subcutaneous), as long as the serum estradiol concentration is sufficiently high (67, 68). Although progestins alone retard loss of bone mass, addition of progestin to estrogen probably is not any more beneficial than estrogen alone (69, 70).

If estrogen use is started several years after menopause, it will protect against loss of bone mass as long as it is administered (66, 71). However, bone lost between menopause and commencement of estrogen use will not be recovered.

One study (72) found that women younger than 75 years of age who had taken estrogen for 7 years or more had higher bone mass than women who had never received estrogen; in women aged 75 years and older, bone mass was almost the same among these two groups of women. Most of the older women who had ever used estrogen had not used it recently, suggesting that recency of use is important.

Many observational epidemiologic studies indicate that estrogen replacement therapy also protects against hip fracture, and that the longer estrogen is used, the greater the protection. A meta-analysis of these observational studies suggests a relative risk of around 0.75 among women who have used estrogen (73). These studies, however, included relatively few women aged 75 years and older. Cauley et al. (74) have reported that the degree of protection against fractures afforded by estrogen is greater among current or recent users, with previous use appearing to give little protection. Available evidence also suggests that women over the age of 75 years who have ever used estrogen are not protected against hip fracture (75–77) or are protected not nearly to the extent of women under the age of 75 years (75, 78). This lack of protection in older women probably occurs because most of these women are previous, not current or even recent, users. Starting estrogen within a few years of the time of menopause appears to give more protection against fractures than starting later (74, 79). The limited available data suggest that combination therapy with estrogen and progestin provides about the same degree of protection against hip fracture as estrogen alone (74, 75).

Reproductive factors

Later age at menopause is associated with reduced risk of hip fracture (46, 76, 80, 81). Johnell et al. (81) recently reported that early age at menarche protected against hip fracture, but no such protective association has been found in other studies (76, 80, 82).

Maternal calcium is needed for the fetal skeleton during pregnancy and for breast milk, suggesting that pregnancy and breastfeeding might lead to reduced maternal bone mass. However, studies that have followed women through pregnancy, breastfeeding, and weaning have found that bone lost during breastfeeding may be restored after weaning (83), suggesting that breastfeeding may have little impact on long-term risk of hip fracture. Indeed, there is no epidemiologic evidence that breastfeeding is associated with an increased risk of hip fracture (46, 80, 84). Neither has any epidemiologic study found a positive association between hip fracture and number of pregnancies (46, 76, 80, 84).

HEALTH STATUS AND MEDICAL CONDITIONS

In recent cohort studies, Cummings et al. (46) found that poorer self-rated health status was a predictor of hip fracture, while Wolinsky and Fitzgerald (47) found no such association. In the latter study, however, hos-
Cognitive impairment

Buchner and Larson (85) found that the risk of fractures, not just hip fractures, among people with Alzheimer’s disease was three times higher than expected. In a prospective study carried out in a cohort of women who lived in nursing homes (39), a threefold increased risk of hip fracture was found when women in the lowest tertile were compared with those in the highest tertile with the use of a test of cognitive function. A prospective study of a cohort of women who lived in the community (46) found a weaker, and not statistically significant, association between cognitive impairment and hip fracture. Confusion, as noted in medical records prior to fracture, was associated with more than a doubling in risk of hip fracture in a case-control study of hip fractures that occurred in hospital (86).

Neuromuscular factors

Studies have consistently demonstrated that impairments of gait, balance, and lower extremity strength are associated with increased risk of falls (87–89). A meta-analysis of the Frailty and Injuries: Cooperative Studies of Intervention Techniques (FICSIT) trials (90) found that exercise programs designed to improve balance and muscle strength reduced the risk of falls by 10 percent.

Muscle weakness, lower limb dysfunction, and use of walking aids (a marker of neuromuscular impairment) have been associated with hip fracture risk in numerous studies (46, 77, 82, 91–95). Importantly, three recent cohort studies (46, 95, 96) found that associations between neuromuscular function and risk of hip fracture were independent of bone mass, confirming the importance of fall-related factors in the etiology of fractures in older people.

Vision

There have been many studies of the relation between visual impairment and frequency of falls, but only a few studies of hip fracture etiology have included a detailed visual examination (46, 95, 97). In the Framingham Eye Study (97), participants were followed for 10 years, and those with poor visual acuity in one or both eyes were at increased risk of hip fracture. Cataracts and diabetic retinopathy were also associated with risk of hip fracture. In the Study of Osteoporotic Fractures (46), poor depth perception and poor contrast sensitivity were related to hip fracture risk, but visual acuity was not. Poor visual acuity was associated with hip fracture in the Épidémiologie de l’ostéoporose (ÉPIDOS) cohort study (95), where women with the worst visual acuity (≤2/10 on a Snellen chart) had twice the hip fracture rate of women with the best vision (>7/10).

Fracture history

People who have had one hip fracture have a 60 percent higher risk of a subsequent hip fracture than people with no history of hip fracture (98, 99). History of distal radial fractures appears to be associated with an increased risk of hip fracture of between 50 and 100 percent (100–103). A similar magnitude of effect is evident in cohort studies of the risk of hip fracture in people with previous proximal humeral (102, 104) or vertebral fractures (105). The associations between fracture history and later hip fracture appear to be stronger in men than in women.

Osteoarthritis

Early case series suggested that osteoarthritis of the hip was uncommon in patients treated for hip fracture (106, 107). Supporting the existence of an inverse association between these two conditions is the finding of high hip bone mass among people in the general population with radiographic evidence of hip and knee osteoarthritis and a greater distal radial and metacarpal cortical bone mass in patients undergoing surgical treatment of hip osteoarthritis (106, 107).

Case-control studies of hip fracture have found a lower rate of self-reported osteoarthritis in cases (108, 109). In contrast, cohort studies have failed to find a lower risk of hip (46) or other fractures (110) in women with self-reported osteoarthritis, and in women with radiographic osteoarthritis of the hip (111). Thus, whether osteoarthritis of the hip or other joints protects against the risk of hip fracture remains uncertain. Such a relation could be indirect, due to the association of greater body weight and physical activity with an increased risk of osteoarthritis and a decreased risk of hip fracture. However, the higher bone mass of women with hip osteoarthritis appears to be independent of these factors.

Other medical conditions

Parkinson’s disease and stroke have been associated with increased risk of hip fracture in several studies (77, 92, 112). These conditions are associated with increased risk of falling and probable reduced bone strength due to poor mobility. People with Parkinson’s disease appear to be at particularly high risk of hip
fracture, with reported relative risks of 10 or more (92, 112).

Studies suggest that epilepsy, gastrectomy, hyperthyroidism, pernicious anemia, and diabetes might be associated with increased risk of hip fracture (46, 113–117).

**MEDICATIONS**

**Psychotropic medications**

Two population-based case-control studies by Ray et al. (118–121) linked data on diagnoses and medication prescriptions in large computerized files. The first of these studies (118) involved Medicaid recipients and found that antipsychotics (relative risk (RR) = 2.0), long-acting hypnotics (RR = 1.8), and tricyclic antidepressants (RR = 1.9) were all associated with an increased risk of hip fracture. These findings were confirmed in a second study (119, 120), based on records of the health insurance system in Saskatchewan, Canada. This study also found that opioid analgesics (codeine and/or propoxyphene) were associated with an increased risk of hip fracture (RR = 1.6) (121).

A problem in any observational study of psychotropics and hip fractures is confounding by indication. It is possible that the conditions (such as dementia) for which the psychotropics were prescribed are the cause of the hip fractures, not the medications themselves.

**Thiazide diuretics**

Thiazide diuretics cause reduced urinary calcium excretion (122). Randomized trials suggest that thiazides might slow the rate of bone loss in postmenopausal women (123, 124). There has been some concern that diuretics might increase the risk of falling (125). However, a randomized trial of antihypertensive therapy (which included a thiazide diuretic) in the elderly found no increased risk of falls among subjects in the treatment arm (126).

In a recent meta-analysis, Jones et al. (127) reported a pooled relative risk of 0.8 for thiazides and risk of hip fracture. Thiazide’s protective effect was only apparent among long-term users. This meta-analysis does not overcome any scientific flaws in the included studies. In particular, uncontrolled confounding is a potential problem in all observational studies of thiazides and hip fracture. Several studies suggest that there may be a tendency for thiazide diuretics to be taken by people at relatively low risk of hip fracture (77, 128, 129). For example, Cumming and Klineberg (129) found that thiazide users were heavier and had better cognitive function than nonusers.

**WEIGHT AND HEIGHT**

Low body weight, adjusted or unadjusted for height, has long been recognized as a risk factor for hip fracture (130). There are four plausible explanations: conversion in adipose tissue of androstenedione to the more active estrone is the major source of active estrogen in postmenopausal women (131), and estrogens reduce the risk of hip fracture; greater weight increases the mechanical strain on bone, stimulating bone remodeling (132); increased soft tissue overlying the greater trochanter reduces the force applied to the proximal femur in a fall; and low body weight can be a marker for poor health status, itself a risk factor for falls and fractures.

An association between change in weight and risk of hip fracture has been observed in recent studies (46, 77, 91, 133, 134). In the Study of Osteoporotic Fractures (46), a 20 percent weight gain between age 25 years and old age was associated with a 40 percent reduction in risk of hip fracture, and weight loss increased fracture risk. These associations were independent of actual weight and bone density. The explanation for these findings is unclear, although weight loss may reflect some underlying illness that increases risk of hip fracture.

Nearly all the studies that have reported the relation between height and hip fractures have found that taller people are at greater risk of hip fracture than shorter people (54, 76, 81, 116, 117, 133, 135–137). The relation between height and hip fracture is independent of weight. Height is strongly correlated with hip axis length, which is associated with increased risk of hip fracture.

Two studies have considered height when subjects were in their twenties (46, 133), and both found a stronger relation for peak height and fracture risk than for current height. Peak height is likely to be more strongly related to aspects of proximal femoral geometry, such as hip axis length, than height in old age because vertebral fractures lead to height loss in many older people.

**DIET**

**Calcium**

The accumulated evidence from randomized trials is that calcium supplements reduce the rate of bone loss in postmenopausal women (138, 139). There has been only one randomized trial of calcium supplements with hip fracture as the outcome (140). The study involved 3,270 French nursing home residents randomized to 1,200 mg of calcium and 20 μg of vitamin D₃ or placebo. There was a 27 percent reduction in hip fracture incidence in the intervention group. Interpre-
tation of this important trial is complicated by the cointervention with vitamin D and the nursing home setting.

The results of randomized trials of calcium supplements and bone mass suggest that high intake of dietary calcium should reduce the risk of hip fracture. Observational epidemiologic studies, however, are far from consistent (46, 76, 81, 82, 91, 94, 117, 133, 141–146). Only three studies (81, 141, 142) show convincing evidence of reduced risk of hip fracture with higher calcium intakes. One of these studies (142) was done among Hong Kong Chinese with a very low average daily calcium intake of 170 mg a day, and another (81) involved women living in southern Europe.

The failure to find a protective effect of dietary calcium for hip fractures in most studies may be because of inadequate measurement of dietary calcium or because the numbers of study subjects may have been too small to detect what is likely to be a relatively small calcium effect.

Alcohol

Alcoholics tend to have low bone mass (147), but this could be due to general nutritional deficiencies rather than a specific alcohol effect. In contrast, recent longitudinal studies of nonalcoholics (148–150) have found that moderate alcohol consumption was associated with higher bone mass. Somewhat surprisingly, there is little epidemiologic evidence that alcohol is associated with falls.

Studies of the relation between usual alcohol consumption and risk of hip fracture are inconsistent. Several studies (77, 82, 142, 151, 152) have found a statistically significant increased risk of hip fracture with higher levels of alcohol intake; however, most cohort studies have found no relation (46, 76, 136, 141). In fact, the Study of Osteoporotic Fractures (46) found a reduced risk of hip fractures in drinkers compared with nondrinkers, a finding largely explained by the better health status of the drinkers in that study.

Conflicting results might be explained by the hypothesis that heavy drinkers are at increased risk of hip fracture, while moderate drinking is protective. A protective effect of alcohol could be mediated via a reduction in risk of cardiovascular disease (leading to reduced frailty and fewer falls); an increase in the conversion of androstenedione to the more active estrogen, estrone (153); or alcohol-induced secretion of calcitonin (147). Another possibility is the phytoestrogens found in some alcoholic beverages.

Caffeine

Caffeine may increase urinary excretion of calcium and so could lead to a reduction in bone mass (154). Studies of caffeine and bone mass are inconsistent. Most recent studies (155–157), but not all (158), have found lower bone mass in people with higher caffeine intakes. Most cohort studies of caffeine intake and hip fracture (46, 152, 159) have found a statistically significant positive association, while case-control studies (81, 117, 133, 144) have tended to find no association. The cohort studies that found positive associations all assessed usual caffeine intake with food frequency type questionnaires; the one negative cohort study (141) used 24-hour recall. This may explain the different findings.

The main sources of caffeine are coffee and tea. Tea contains fluoride and phytoestrogens, both of which might reduce fracture risk. Tea consumption was associated with a statistically significant reduction in risk of hip fracture in the recent Mediterranean Osteoporosis Study (MEDOS) (81). In other studies that considered tea and coffee separately (133, 144, 152), tea drinking was associated with a nonsignificant reduced risk of fracture and coffee drinking with an increased risk of fracture. For example, in the Nurses Health Study (152), women who drank four or more cups of coffee a day had a threefold increased risk of hip fracture compared with nondrinkers of coffee; whereas drinkers of two or more cups of tea a day had a 30 percent lower risk of hip fracture than nondrinkers of tea.

Other dietary factors

The catabolism of dietary protein leads to a mild metabolic acidosis that may be counteracted by the release of calcium salts from bone (160). A recent randomized trial (161) showed that administration of potassium bicarbonate (which neutralizes acid) to postmenopausal women led to improved calcium balance, reduced bone resorption, and increased bone formation. These data suggest that high levels of dietary protein could increase the risk of hip fracture. There is a strong positive correlation between a country’s average protein consumption and its hip fracture incidence (162); however, no study to date with individual level data on protein intake and hip fractures has found an association (117, 144, 163, 164).

A recent Swedish study (117) found statistically significant associations between higher intakes of dietary iron, magnesium, and vitamins A and C and increased risk of hip fracture. An earlier study of vitamin C intake (144) found no association with hip fracture.
PHYSICAL ACTIVITY

Physical activity could influence risk of hip fractures through the skeletal fragility and/or falls etiologic pathways. Randomized trials of physical activity and bone mass (165, 166) have produced conflicting results. A problem with most of these trials has been poor compliance with the exercise program, with 40 percent or more of randomized participants dropping out. There is some evidence from randomized trials that exercise can improve balance and muscle strength (167–169), and the FICSIT trials provide direct evidence that exercise can reduce the risk of falls (90, 170).

Observational studies (46, 76, 81, 82, 91, 93, 94, 116, 117, 133, 142, 145, 171, 172) have consistently found that physical inactivity in old age is associated with increased risk of hip fracture. Studies that have investigated recalled physical activity many years in the past (81, 142, 144, 145, 173–175) have also tended to find that past physical inactivity is associated with increased fracture risk. For example, a sedentary job at age 50 years (such as being a secretary) was associated with a three times higher risk of later hip fracture than doing a job that involved a combination of sitting and walking (such as teaching) (173).

At least part of the explanation for the observed associations between physical inactivity and hip fracture could be that physical inactivity lies on the causal pathway between poor health and hip fracture. On the other hand, existence of a causal relation is supported by randomized trials suggesting that exercise might be beneficial for bone mass, balance, and muscle strength.

SMOKING

Smoking may cause changes in the metabolism of hormones that affect bone strength (176). Smokers have lower bone mass than nonsmokers (155, 177–181). Most studies of smoking and hip fracture (46, 76, 77, 82, 91, 94, 116, 117, 133, 142, 143, 172, 182–184), but not all (81, 136, 141, 145, 151), have found that smokers are at greater risk of hip fracture than nonsmokers. The relative risks for hip fracture in smokers compared with nonsmokers have all been between 1.0 and 2.7, except in one study (94) which found a relative risk of 5.6.

The observed increased risk of hip fractures in smokers does not appear to be explained by a tendency for smokers to have lower body weight and earlier age at menopause, because adjusting for these potential confounders does not greatly reduce relative risks (133). It may be that smokers are generally less healthy than nonsmokers and their poor health increases their risk of falling. In the Study of Osteoporotic Fractures (46), adjusting for poor self-rated health and various measures of neuromuscular function attenuated the hip fracture-smoking relative risk from 2.1 to 1.4.

OTHER RISK FACTORS

Environmental hazards

Environmental hazards are usually included in any list of risk factors for falls and fractures. However, studies of home hazards and falls have tended to find only modest differences between the homes of fallers and nonfallers (87–89, 185). To our knowledge, there has only been one published study of environmental hazards and hip fractures (186). Although several associations were noted in this case-control study, the authors attributed these associations to biased data collection (186).

Fluoride

Fluoride stimulates bone formation (187). Ecologic studies that have compared hip fracture rates in areas with varying levels of fluoride in drinking water (188–190) have produced conflicting results. Comparisons of hip fracture rates before and after fluoridation of a community’s drinking water are also inconsistent (191). In a recent cohort study with individual level data on fractures and duration of exposure to a fluoridated water supply (but not amount of water consumed) (192), there was no association between fluoridated water and hip fractures.

Vitamin D

Vitamin D is an important hormone for regulation of bone metabolism. Gross deficiency of vitamin D causes osteomalacia and muscle weakness (193), and so it might be expected that inadequate vitamin D levels would increase the risk of hip fracture. Several studies (e.g., 194, 195) have found that serum vitamin D levels are lower in patients with hip fractures than in controls, and a recent case-control study (91) found that low dietary vitamin D intake was associated with increased risk of hip fracture. The success of Chapuy et al. (140) in reducing hip fracture rates in French nursing home residents with a combination of vitamin D and calcium supplements could have been due to vitamin D and not calcium. However, a randomized trial that involved older people living in the community (196) found no effect of a vitamin D supplement on hip fracture rates.

SUMMARY AND PRIORITIES FOR FUTURE RESEARCH

Established risk factors for hip fracture in women are shown in Table 1. These include low bone mineral density, history of falls, direction of fall, neuromuscular impairment, weight, white race, use of hormone replacement therapy, and ultrasound attenuation. While assessment of many of these factors is clearly useful for quantifying an individual's risk of hip fracture, research is needed on pharmacologic approaches to increasing bone mass (with fractures as endpoints) and identification of the most effective exercise programs for improving muscle strength and balance. Methods of reducing the force applied to the femur in a fall on the hip, such as external hip protectors, need further evaluation. Many important questions about hormone replacement therapy still need to be resolved, including the best time to start (at menopause or later) and whether or not a woman needs treatment for the rest of her life if she is to be protected against hip fractures at the ages at which they are most likely to occur.

Table 2 shows factors that are likely to be risk factors for hip fracture, but about which some uncertainty still exists. Psychotropic medications and thiazide diuretics are included in this category because it is possible that confounding by indications for prescribing these medications could explain the observed associations. This bias can only be avoided by evaluation of these medications in randomized trials. Randomized trials of thiazides are feasible and should be done. Although randomized trials designed specifically to evaluate the effects of psychotropics on risk of fracture are not possible, recording falls as one outcome in randomized trials of new psychotropic medications is recommended.

Most studies have found that physical inactivity is associated with increased risk of hip fracture, but this could be due to confounding by health status. Nevertheless, because exercise protects against cardiovascular disease, and it may well improve general physical and mental health, it seems reasonable to promote physical activity as a means of hip fracture prevention. Further research on physical activity should focus on identification of the specific activities that are most strongly associated with hip fracture.

The evidence suggests that smoking probably increases the risk of hip fracture. A meta-analysis might be useful for identifying reasons for the few discrepant study findings and for quantifying the magnitude of the hip fracture-smoking association. New research on smoking and hip fracture is probably not warranted, given the overwhelming evidence that smoking is harmful to health.

The consistent finding from randomized trials that calcium supplementation leads to reduced bone loss suggests that more dietary calcium may well reduce risk of hip fracture. Despite the inconclusive results of observational studies, increasing dietary intake of calcium is probably a prudent clinical and public health

| TABLE 1. Established risk factors for hip fracture in women |
|---|---|
| **Relative risk ≥ 2.0** |
| Bone mineral density of the femur | Per 1 SD* decrease |
| Fall on hip | Fall on hip vs. fall on other part of body |
| Neuromuscular impairment | Unable to rise from chair without using arms vs. able to rise from chair |
| Race | Whites vs. Asians (in Asia) |
| Ultrason attenuation | Per 1 SD decrease |

| **Relative risk 1.1 to 1.9** |
| Age | Per 5 year increase |
| Bone mineral density at nonfemoral sites | Per 1 SD decrease |
| Falls in past year | ≥ 2 falls vs. 0 falls |
| Hormone replacement therapy | Nonusers vs. users |
| Neuromuscular impairment | Grip strength | Per 5 kg decrease |
| Gait speed | Per 0.2 m/sec decrease |
| Weight | Per 10 kg decrease |

*SD, standard deviation.

| TABLE 2. Factors found to be risk factors for hip fracture in several studies, but about which some uncertainty still exists |
|---|---|
| **Risk factor** | **Comparison** |
| Health status | Poor/fair vs. good/excellent |
| Parkinson's disease | Present vs. absent |
| Race | Whites vs. Hispanics |
| Weight change | 20% weight loss |
| **Relative risk 1.1 to 1.9** |
| Coffee | >2 cups/day vs. no coffee |
| Calcium intake | <400 mg/day vs. >1,000 mg/day |
| Fractures since age 50 years | Fracture vs. no fractures |
| Height | Per 10 cm increase |
| Hip axis length | Per 1 SD* increase |
| Psychotropic drugs | Users vs. nonusers |
| Smoking | Smokers vs. nonsmokers |
| Thiazides | Nonusers vs. users |
| Vision | Acuity worse than 20/40 |
| Physical inactivity | Not walking for exercise vs. walking for exercise |

*SD, standard deviation.
policy. A more definitive conclusion will have to await the findings of the ongoing Women's Health Initiative randomized trial of calcium plus vitamin D for hip fracture prevention being conducted at sites across the United States.

Table 3 shows factors that might be related to risk of hip fracture but for which current evidence is of only moderate or poor quality. Some of these factors—alcohol, dementia, family history of fractures, fluoride, osteoarthritis, and dietary protein and vitamins A and C—should be the focus of further observational studies. The role of biochemical markers of bone turnover for prediction of hip fracture also needs much more study (197). The effect of fluoride should be also studied in randomized trials, given the great difficulty of measuring fluoride intake at the individual level. The importance of hazards in the home environment is probably also best studied in the context of a randomized trial of hazard reduction, with falls as endpoints.

Tables 1 and 2 show estimates of the strength of association between various risk factors and risk of hip fracture. Strength of association depends to some extent on a risk factor's position on the causal pathway. Thus, assessment of skeletal fragility by bone densitometry would be expected to be more strongly related to risk of hip fracture than calcium intake. Similarly, the association between hip fracture and tests of balance is likely to be stronger than the association with use of psychotropic medications. This implies that direct measurement of skeletal fragility and risk of fall-related trauma will be much better predictors of hip fracture in individual people than assessment of more distant risk factors. At a population level, however, these more distant risk factors could have great importance. For example, about 20 percent of hip fractures (population attributable risk) would be due to smoking in a population where 30 percent of people are smokers (assuming a relative risk just under 2.0 for smoking and hip fracture).

To date, there have only been four randomized trials of hip fracture prevention (57, 140, 196, 198). These trials suggest that, in nursing home residents, external hip protectors and a combination of supplemental calcium and vitamin D can each reduce the risk of hip fracture by about 50 percent. Alendronate, a drug that increases bone density, also appears to be protective (198). Observational epidemiologic studies over the past 10 years have contributed greatly to our understanding of hip fracture etiology. The main challenge now is to use the findings of this research to develop, and evaluate, effective programs for prevention of hip fractures.

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### TABLE 3. Factors that may be risk factors for hip fracture but the quality of current evidence is only moderate or poor

<table>
<thead>
<tr>
<th>Quality of evidence and factor</th>
<th>Moderate quality evidence</th>
<th>Poor quality evidence</th>
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<tbody>
<tr>
<td>Alcohol</td>
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<td>Fluoride</td>
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<td>Dementia</td>
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<td>Home hazards</td>
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<tr>
<td>Family history of hip fracture</td>
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<td>Protein intake</td>
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<td>Markers of bone turnover</td>
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<td>Vitamins A, C, and D</td>
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<td>Osteoarthritis</td>
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