Prospective study of dietary protein intake and risk of hip fracture in postmenopausal women[1–3]

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ABSTRACT

Background: The role of dietary protein intake in osteoporosis remains controversial. Protein is an important structural component of bone and protein supplementation improves the medical outcome of hip fracture patients, but it is unknown whether protein intake can reduce the incidence risk of hip fracture.

Objective: The relation between intake of protein and other nutrients and subsequent incidence of hip fracture was evaluated.

Design: Nutrient intake was assessed with a food-frequency questionnaire in a cohort of Iowa women aged 55–69 y at baseline in 1986. Incident hip fractures were ascertained through follow-up questionnaires mailed to participants in 1987 and 1989 and verified by physician reports.

Results: Forty-four cases of incident hip fractures were included in the analyses of 104 338 person-years (the number of subjects studied times the number of years of follow-up) of follow-up data. The risk of hip fracture was not related to intake of calcium or vitamin D, but was negatively associated with total protein intake. Animal rather than vegetable sources of protein appeared to account for this association. In a multivariate model with inclusion of age, body size, parity, smoking, alcohol intake, estrogen use, and physical activity, the relative risks of hip fracture decreased across increasing quartiles of intake of animal protein as follows: 1.00 (reference), 0.59 (95% CI: 0.26, 1.34), 0.63 (0.28, 1.42), and 0.31 (0.10, 0.93); *P* for trend = 0.037.

Conclusion: Intake of dietary protein, especially from animal sources, may be associated with a reduced incidence of hip fractures in postmenopausal women. *Am J Clin Nutr* 1999;69:147–52.

KEY WORDS Aging, diet, epidemiology, hip fractures, nutrition, osteoporosis, prospective studies, protein intake, postmenopausal women

INTRODUCTION

Osteoporotic hip fractures are a serious and growing burden in North America and Europe and an emerging problem in developing countries. The risk of hip fracture in the remaining lifetime of a 50-y-old woman in North America has been estimated to be 17.5% (1). The total cost per year of osteoporotic fractures, mostly hip fractures, has been estimated to be $10–20 billion in the United States (2). One-half of the world's 1.66 million hip fractures occurred in North America and Europe in 1990, but by 2050 an estimated 70% of the 6.26 million projected annual hip fractures will occur in Asia, Latin America, the Middle East, and Africa as a result of the increasing size and relative age of populations in developing countries (3).

Despite advances in our understanding of the causes of osteoporotic hip fractures, including the roles of estrogen use, calcium intake, body size, bone density, and propensity for falls, greater knowledge of preventive measures is needed to reduce the growing burden (4). Long-term estrogen use reduces bone loss and fracture risk in the 7–10-y period after menopause, but may have little residual effect on bone density and fracture risk among women older than 75 y, who now outnumber younger women in cases of hip fracture by 3 to 1 (5). Calcium and vitamin D supplementation are the leading nutritional interventions for osteoporosis yet are far less effective in preserving bone than is use of postmenopausal estrogen (6). Other nutrients have received far less attention.

The relation between dietary protein intake and osteoporosis is controversial because protein intake has been implicated in negative calcium balance and bone loss in some studies (7–10) but not others (11–13). Low protein intake may compromise bone quality, especially in the elderly (14–16). Protein supplementation improves the medical outcome of hip fracture patients (17), but it is unknown whether protein intake can reduce the incidence of hip fracture. We examined the association between dietary intake of protein and other nutrients and the incidence of hip fracture in a prospective study of older Iowa women.

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SUBJECTS AND METHODS

The Iowa Women's Health Study is a prospective study of cancer incidence to which the present ancillary study of hip fracture was added. All procedures were reviewed and approved by institutional review boards. Iowa women aged 55–69 y in 1986 were selected randomly from the driver's license data files of the Iowa Department of Transportation. This Midwestern state has a population that is 99% white from urban and rural areas. A baseline questionnaire was mailed in January 1986 to 99 826 women and 41 837 women (42%) responded. Other details, including the characteristics of nonrespondents, are published elsewhere (18).

Data collection at baseline

The food-frequency questionnaire (FFQ) used in the 1986 baseline survey was adapted from the Nurses' Health Study (19) and included 127 food items and questions on the use of nutritional supplements (20). Participants reported their patterns of dietary intake over the preceding 12 mo by indicating their usual frequency of consumption of a specified portion size of each food item. The FFQ was found to be reproducible on repeated administration and accurate compared with dietary recall interviews. Participants for whom data were missing for >29 food items or for whom total energy intakes were implausible (<2.5 MJ/d or >20.9 MJ/d) were excluded (20).

Reproductive characteristics assessed at baseline included ages at menarche, first pregnancy, and menopause; number of pregnancies; and use of estrogen. Height and weight were self-reported. Circumferences of the wrist, waist, and hip were measured with the assistance of a family member or friend by using a measuring tape given to each participant; these measurements have been shown to be reliable and valid (21). Waist-to-hip ratio and body mass index (in kg/m^2) were calculated.

Smoking history was classified as ever compared with never smoked and current compared with former smoker. Data on alcohol use were collected in the FFQ and expressed as ethanol use in g/d. Physical activity was characterized with questions regarding regular, moderate, and vigorous physical activities and these data were combined in an index that was found previously to predict coronary artery disease mortality (18).

Identification and validation of hip fractures

Follow-up questionnaires were mailed in 1987 and 1989 with response rates of 91% and 90%, respectively, to collect data on vital status, residence, and self-reported medical conditions and included a brief question on the occurrence of bone fractures. A more detailed fracture questionnaire was later sent to each participant who had reported a fracture. Participants were asked to provide more information on their fracture and consent for the release of medical records. Physicians were then contacted for verification of the fracture and its circumstances. Women who had reported at baseline a history of fractures of the upper arm, forearm, wrist, ribs, or hip after the age of 35 y were excluded because they represented possible prevalent cases of osteoporosis and may have subsequently altered their diet and behavior. Incident fractures caused by high-impact trauma (such as motor vehicle accidents) or neoplasia were excluded.

Statistical analyses

The dietary data were analyzed by using the computer programs and nutrient database provided by the Nurses' Health Study. Nutrient scores were calculated per MJ for each participant and quartiles for the entire cohort were used to define exposure. Nutrient analyses were also performed by regression adjustment of nutrient scores for total energy intake (19), but the results differed little from those presented here. Within each food group the number of servings per MJ was calculated for each participant.

Analyses were restricted to the 32 050 participants (76.6%) who had completed one or both of the follow-up questionnaires and had acceptable dietary data. Person-years of follow-up (the number of subjects studied times the number of years of follow-up) were counted from 1 February 1986 to the date of hip fracture for confirmed cases or to the date of the last completed follow-up questionnaire for others. Person-years and hip fractures were tabulated for each of the nutrient exposure categories and incidence rates were calculated. Relative risks were calculated by using the lowest nutrient quartile as the reference intake and dividing the incidence at each successively higher quartile by the incidence at the reference quartile. The relative risks were age-adjusted by the Mantel-Haenszel procedure (22) by using 5-y age categories. Proportional hazards models of SAS statistical programs (23) were used to control for the possible confounding effects of age, parity, body mass index, smoking, alcohol use, estrogen use, and physical activity. Ninety-five percent CIs were estimated for all relative risks.

RESULTS

Hip fractures were reported in the initial follow-up questionnaire by 125 women who had been free of other fractures since the age of 35 y. Of these, 13 (10.4%) were excluded because of inadequate completion of the dietary questionnaire. The detailed fracture questionnaire was returned by 75 (67.0%) of the remaining women and 66 of these (88.0%) confirmed their original brief report of hip fracture. Women who denied their original report were contacted by telephone and most replied that they had either incorrectly marked the previous questionnaire or had initially mistaken sprains or other pains for fractures. Of the 66 reports verified by subjects, 6 were excluded because of high-impact trauma and 2 were excluded because of complications related to cancer treatment. Of the 58 remaining cases, 44 of the women's physicians (75.9%) responded to the request for validation and in each of these 44 cases the hip fracture was confirmed by the physician.

Baseline data on age and reproductive, anthropometric, and lifestyle characteristics of cohort members with and without subsequent hip fractures are shown in **Table 1**. Women with subsequent hip fractures were older than the others (P = 0.006), slightly younger at menopause, and older at their first pregnancy, although these last 2 differences were not significant. The mean number of pregnancies was significantly less in the hip fracture group (P < 0.001). Women with hip fractures weighed less at baseline (P = 0.008) and were taller and thus had a lower body mass index (P < 0.001) than the others. Women in the hip fracture group also had smaller mean circumferences of the waist (P = 0.02) and hip (P = 0.04), indicating their leaner characteristics compared with the others. The distribution of body fat as indicated by the waist-to-hip ratio was not significantly different between the 2 groups. The number of women who were current or past smokers did not differ significantly between groups; additionally, women who subsequently had a hip fracture were less physically active and used estrogen less often, although these 2 differences were not significant.

TABLE 1
Characteristics at baseline of participants in the Iowa Women's Health Study with and without subsequent hip fracture

Characteristic	No hip fracture (n = 32 006)	Hip fracture (n = 44)
Age (y)	61.4 ± 4.2[1]	63.2 ± 4.7[2]
Age at menopause (y)	47.7 ± 6.4	47.0 ± 7.9
Age at first pregnancy (y)	22.6 ± 4.0	23.3 ± 3.9
Number of pregnancies	3.9 ± 2.2	3.1 ± 1.5[3]
Weight (kg)	69.3 ± 13.5	63.9 ± 11.4[4]
Height (cm)	162.8 ± 6.4	164.3 ± 6.9
Body mass index (kg/m^2)	27.0 ± 5.1	24.4 ± 3.7[5]
Wrist circumference (cm)	16.0 ± 1.3	15.7 ± 1.3
Waist circumference (cm)	87.9 ± 14.0	83.6 ± 10.9[6]
Hip circumference (cm)	104.6 ± 10.9	101.3 ± 9.1[7]
Waist-to-hip ratio	0.84 ± 0.09	0.82 ± 0.06
Current smoker (%)	14.5	13.6
Ever smoked (%)	19.6	20.5
Current estrogen user (%)	12.0	5.0
Ever used estrogen (%)	38.0	30.0
Physical activity index (%)		
Low	47.0	57.0
Moderate	28.0	23.0
High	25.0	20.0

[1] $\bar{x}$ ± SD.
[2–7] Significantly different from group with no subsequent hip fracture: [2] P = 0.006, [3] P = 0.0008, [4] P = 0.008, [5] P = 0.0001, [6] P = 0.02, [7] P = 0.04.

TABLE 2
Mean total energy intake and nutrient intakes per MJ at baseline of participants in the Iowa Women's Health Study with and without subsequent hip fracture[1]

Nutrient intake	No hip fracture (n = 32 006)	Hip fracture (n = 44)
Total energy (MJ)	7.53 ± 2.53	7.34 ± 2.53
Protein (g/MJ)	10.85 ± 1.98	10.11 ± 1.65[2]
Animal protein (g/MJ)	7.96 ± 2.17	6.96 ± 1.84[3]
Vegetable protein (g/MJ)	2.92 ± 0.65	3.15 ± 0.67[2]
Carbohydrate (g/MJ)	28.85 ± 4.54	30.54 ± 4.33[2]
Animal fat (g/MJ)	5.19 ± 1.46	4.68 ± 1.31[4]
Vegetable fat (g/MJ)	3.85 ± 1.24	4.09 ± 1.08
Saturated fat (g/MJ)	3.23 ± 0.67	3.06 ± 0.72
Polyunsaturated fat (g/MJ)	1.65 ± 0.43	1.67 ± 0.36
Monounsaturated fat (g/MJ)	3.35 ± 0.65	3.23 ± 0.65
Dietary calcium (mg/MJ)	111.93 ± 42.78	105.93 ± 36.33
Calcium from supplements (mg/MJ)	42.95 ± 64.84	49.67 ± 98.80
Total calcium (mg/MJ)	153.92 ± 77.17	155.57 ± 105.45
Dietary vitamin D (IU/MJ)	34.06 ± 18.00	33.53 ± 16.80
Vitamin D from supplements (IU/MJ)	23.16 ± 42.52	27.87 ± 48.26
Total vitamin D (IU/MJ)	57.19 ± 46.68	61.40 ± 50.00
Phosphorus (mg/MJ)	174.33 ± 35.73	167.83 ± 29.73
Alcohol (g/MJ)	0.55 ± 1.27	0.45 ± 1.05

[1] $\bar{x}$ ± SD.
[2–4] Significantly different from group with no subsequent hip fracture: [2] P = 0.01, [3] P = 0.002, [4] P = 0.02.

Mean total daily energy and nutrient intakes per MJ at baseline for women with and without subsequent hip fractures are shown in **Table 2**. Total energy intake was not significantly different between the 2 groups. The hip fracture group did have a lower mean daily intake of total protein (P = 0.01) that represented a lower intake of animal protein (P = 0.002) but a higher intake of vegetable protein (P = 0.01). The women with hip fractures also had lower intakes of animal fat (P = 0.02) and higher intakes of carbohydrate (P = 0.01) than the others. The intakes of other types of fat, dietary and supplemental calcium and vitamin D, phosphorus, and alcohol were not significantly different between the 2 groups.

The nutritional analyses were extended to food items (**Table 3**). Fruit and vegetable consumption was not significantly different between the 2 groups. Women with subsequent hip fractures had a lower mean consumption of most of the high-protein foods, including milk, all dairy products, red meat, and all meat items combined. These differences were only significant, however, for red meat (beef, pork, and lamb; P = 0.05) and all meat combined (P = 0.03).

The age-adjusted relative risks of hip fracture according to quartiles of nutrient intake are shown in **Table 4**. The relative risk of hip fracture decreased with increasing total protein intake (P for trend = 0.006) and this appeared to result from a strong association with animal rather than vegetable protein. Intake of animal protein was negatively associated (P for trend = 0.002) and intake of vegetable protein was positively associated (P for trend = 0.02) with hip fracture risk. Hip fracture risk also increased with increasing quartile of carbohydrate intake (P for trend = 0.02). Similar analyses revealed no significant associations between intakes of total fat, saturated fat, calcium, and vitamin D and risk of hip fracture (data not shown).

The potential confounding effects of age, number of pregnancies, body mass index, smoking, alcohol use, estrogen use, and physical activity were examined in multivariate analyses by using Cox proportional hazards models. When these variables were included in the model, the risk of hip fracture in the highest quartile of animal protein intake was 31% of the risk at the lowest quartile of intake (relative risk: 0.31, 95% CI: 0.10, 0.93; P for trend = 0.037). In the multivariate analysis, vegetable protein was positively associated with hip fracture risk, but not significantly so (P for trend = 0.11); the association with carbohydrate intake was also diminished and the lack of association with total fat, saturated fat, calcium, and vitamin D intakes remained unchanged (data not shown).

TABLE 3
Mean intake of food items per MJ by food group at baseline by participants in the Iowa Women's Health Study with and without subsequent hip fracture[1]

Food group	No hip fracture (n = 32 006)	Hip fracture (n = 44)
	no. of servings	
Fruit	0.34 ± 0.19	0.37 ± 0.19
Vegetables	0.40 ± 0.24	0.41 ± 0.22
Cruciferous vegetables	0.06 ± 0.05	0.05 ± 0.03
Legumes	0.05 ± 0.04	0.05 ± 0.03
Milk	0.15 ± 0.14	0.12 ± 0.13
All dairy products	0.51 ± 0.27	0.48 ± 0.21
Chicken and turkey	0.03 ± 0.03	0.03 ± 0.03
Beef, lamb, or pork	0.14 ± 0.07	0.11 ± 0.06[2]
Fish	0.03 ± 0.03	0.03 ± 0.03
All meat	0.20 ± 0.08	0.17 ± 0.06[3]

[1] $\bar{x}$ ± SD.
[2,3] Significantly different from group with no subsequent hip fracture: [2] P = 0.05, [3] P = 0.03.

TABLE 4
Relative risk of hip fracture, according to quartile of total protein, animal protein, vegetable protein, and carbohydrate intake among participants in the Iowa Women's Health Study

Quartile of nutrient intake	No. of hip fracture cases	Total person-years[1]	Age-adjusted relative risk (95% CI)	Chi-square for trend (P value)	Multivariate-adjusted relative risk (95% CI)[2]	Chi-square for trend (P value)
Total protein (g/MJ)						
Q1: <9.56	16	26008	1.00		1.00	
Q2: 9.56–10.78	16	26131	1.02 (0.51, 2.05)		0.96 (0.45, 2.06)	
Q3: 10.78–12.05	7	26121	0.44 (0.18, 1.07)		0.46 (0.18, 1.21)	
Q4: >12.05	5	26078	0.33 (0.12, 0.89)	0.006	0.44 (0.16, 1.22)	0.049
Animal protein (g/MJ)						
Q1: <6.48	20	26015	1.00		1.00	
Q2: 6.48–7.82	10	26138	0.50 (0.24, 1.08)		0.59 (0.26, 1.34)	
Q3: 7.82–9.26	10	26077	0.51 (0.24, 1.10)		0.63 (0.28, 1.42)	
Q4: >9.26	4	26108	0.21 (0.07, 0.63)	0.002	0.31 (0.10, 0.93)	0.037
Vegetable protein (g/MJ)						
Q1: <2.51	7	26028	1.00		1.00	
Q2: 2.51–2.88	7	26082	0.99 (0.35, 2.81)		1.15 (0.38, 3.42)	
Q3: 2.88–3.28	13	26124	1.80 (0.72, 4.51)		1.86 (0.69, 4.98)	
Q4: >3.28	17	26104	2.24 (0.92, 5.40)	0.02	1.92 (0.72, 5.11)	0.11
Carbohydrate (g/MJ)						
Q1: <25.97	4	26037	1.00		1.00	
Q2: 25.97–28.87	12	26144	2.79 (0.90, 8.61)		2.58 (0.81, 8.19)	
Q3: 28.87–31.94	11	26056	2.39 (0.76, 7.51)		1.73 (0.51, 5.87)	
Q4: >31.94	17	26102	3.53 (1.20, 10.40)	0.02	2.99 (0.96, 9.35)	0.11

[1] Number of subjects studied in each quartile times the number of years of follow-up.
[2] Covariates in the proportional hazards models included age, body mass index, number of pregnancies, smoking, alcohol use, estrogen use, and physical activity.

DISCUSSION

Protein from animal sources was the nutrient variable with the strongest negative association with risk of hip fracture in this prospective study of Iowa women. Protein from vegetable sources did not appear to protect against hip fractures. The food-group analyses added some consistency to the protein findings because women who later suffered a hip fracture consumed on average fewer servings of foods in each of the high-protein food groups than did the other women. Calcium and vitamin D intake were not associated with hip fracture risk and although carbohydrate intake was initially positively associated, this association was diminished in the multivariate analysis.

Analyses based on single nutrients derived from dietary questionnaires must be interpreted with caution because of the collinearity of nutrient intakes. Animal and vegetable protein intakes were negatively correlated ($r = -0.43$, $P < 0.0001$) and each had a different pattern of correlations with other nutrients. Animal protein intake was positively correlated with dietary calcium ($r = 0.32$, $P < 0.0001$), saturated fat ($r = 0.30$, $P < 0.0001$), and vitamin D intake ($r = 0.28$, $P < 0.0001$) and was negatively correlated with intakes of carbohydrate ($r = -0.56$, $P < 0.0001$) and polyunsaturated fat ($r = -0.24$, $P < 0.0001$). Vegetable protein intake was positively correlated with intakes of carbohydrate ($r = 0.44$, $P < 0.0001$) and polyunsaturated fat ($r = 0.17$, $P < 0.0001$) and negatively correlated with intakes of saturated fat ($r = -0.30$, $P < 0.0001$) and monounsaturated fat ($r = -0.29$, $P < 0.0001$). The small number of verified hip fractures did not allow analyses of nutrient interactions.

The discrepant findings for animal compared with vegetable sources of protein intake and risk of hip fracture have several possible explanations. The largest share of total protein intake in the Iowa women was derived from animal (73%) and not vegetable (27%) sources; additionally, vegetable protein intake was negatively correlated with total protein intake ($r = -0.15$, $P < 0.0001$). A beneficial effect of vegetable protein intake on hip fracture risk may exist but may have been difficult to detect because of the relatively low intake of vegetable protein intake in the Iowa population and the inverse relation between vegetable protein intake and total protein intake. Differences in protein quality and availability between animal and vegetable sources, related to amino acid distribution or associated dietary constituents with effects on digestibility, absorption, and metabolism of amino acids, may underlie the different associations between animal and vegetable protein intake and risk of hip fracture. An alternative interpretation is that an unrecognized, nonprotein constituent of animal-derived foods may explain the observed association between animal protein intake and risk of hip fracture.

The role of poor nutrition in hip fracture was noted as early as 1824 by Sir Astley Cooper, who described the atrophic skeletal state of patients admitted to London hospitals with hip fractures (24). Malnutrition is well established as a cause of poor bone development and maintenance (25) and may contribute to medical complications of hip fracture patients. Delmi et al (26) showed that a daily dietary supplement significantly reduced complications and mortality from hip fracture. In addition to direct effects on bone, malnutrition may increase fracture risk by increasing the likelihood of falls as a result of impaired reaction time and reduced muscle strength and coordination. Vellas et al (27) found that elderly patients who had suffered falls had reduced muscle mass and a poorer profile of serum proteins compared with similar patients who had not fallen. A prospective study of white women in the first National Health and Nutrition Examination Survey found that reduced serum albumin, a sensitive indicator of poor nutritional status, was associated with risk of subsequent hip fracture (28).

Calcium has been the nutritional focus of osteoporosis research over the past 3 decades, although the results have been controversial (29). In many (4, 30) but not all (31) prospective studies, no relation was found between calcium intake and risk of hip fracture. In nonexperimental studies, separate analysis of calcium is an oversimplification because calcium intake may be associated with high intakes of protein and other nutrients (31). The emerging consensus from clinical trials is that older women benefit by supplementation with calcium, vitamin D, or both through reduced age-related bone loss and fracture risk (29). The longer term (5–10 y) effects of calcium and vitamin D supplementation in preventing hip fractures in the elderly are unknown and warrant the continuation of intervention trials for longer periods.

The preoccupation to date with calcium has resulted in less emphasis on the role of other nutrients in bone quality and osteoporosis. Even though protein is a major structural component of bone, protein intake has been viewed largely in terms of how it influences calcium balance. Wachman and Bernstein (7) proposed that the large amount of meat in the Western diet is a primary source of acid ash, which results in the acidification of urine and a lifelong drain on the buffering capacity of the basic salts of bone, and recommended that alkaline ash be increased in the diet through increased consumption of fruit, vegetables, vegetable protein, and milk. Other authors have echoed this view (8–10). In contrast, Spencer et al (11) found that commonly consumed complex dietary proteins with a high phosphorous content do not cause calcium loss in adults and that in fact diets low in protein and phosphorus may have adverse effects on calcium balance in the elderly. Lutz and Linkswiler (12) found in a metabolic study of postmenopausal women that increased protein intake significantly increased net calcium absorption and urinary calcium excretion.

Several lines of evidence from many but not all epidemiologic studies point to a role for dietary protein in bone health. Dietary protein intake was positively associated with bone mineral density of the femoral neck and lumbar spine in a study of elderly Swiss patients (32) and with bone mass of the distal radius and proximal femur in premenopausal women in the United States (33). In Japanese women, current protein intake was positively associated with midradial bone mineral content (13). A survey of postmenopausal vegetarian women in Taiwan found that long-term adherents to a vegan vegetarian diet had a 2.5-fold higher risk of falling below a bone mineral density threshold for fracture risk of the lumbar spine and a 4-fold higher risk of being classified as having osteopenia of the femoral neck than did women consuming a less strict vegetarian diet (34). Orwoll et al (35) reported that serum albumin concentrations were positively associated with bone mineral content in men. In a clinical trial, protein supplementation was found to lower rates of complications and death in elderly patients with hip fractures (17). In contrast, animal protein intake had a modest positive association with risk of forearm fracture and no significant association with hip fracture among participants in the Nurses' Health Study (36), in which the median age at fracture was 60 y. Fracture risks may vary by site of fracture and differ by age.

The mechanism by which dietary protein intake may strengthen bone is unclear, but an effect on the structure and function of bone-related proteins is plausible. Dietary protein restriction in ovariectomized rats results in a marked decrease in the α1 type 1 collagen messenger RNA in bone tissues (37). The amino acid lysine is involved in the cross-linking of both collagen and osteopontin, and abnormalities in the hydroxylation of lysine residues in collagen fibers have been described in osteoporotic bone (38). Patients with lysinuric protein intolerance have defective transport of cationic amino acids, decreased collagen synthesis, radiographic evidence of osteoporosis, and an elevated risk of fractures (39); this rare metabolic disorder may provide a clue that lysine and other amino acids play an important role in bone health in the general population. Dietary supplements of lysine have also been shown to increase the intestinal absorption and renal conservation of calcium (40). Cereal grains and legumes are generally poor sources of lysine (41) and this fact may help to explain the observation that risk of hip fracture was positively associated with vegetable protein intake but negatively associated with animal protein intake in Iowa women.

The prospective nature of the Iowa study and the exclusion of prevalent fracture cases precluded biased recall of diet and other characteristics. The initial, brief self-reports of fractures, made in the context of a broad follow-up questionnaire, seemed inadequate for the accurate identification of hip fracture cases. Thus, a further strength of the study was the use of a more detailed fracture questionnaire to verify the initial reports and physician validation of the reported hip fractures. Although these verification steps ensured that the fracture cases used in the analyses were valid, the possibility exists that the remaining validated cases were not representative of all persons with hip fractures in this population. An examination of demographic characteristics of the physician-verified cases of hip fracture compared with the unverified cases did not reveal evidence of bias in the selection of the verified cases: the mean baseline age, height, and educational attainment of the 2 groups were not significantly different. The mean weight of the unverified cases (67.4 kg) was greater than that of the verified cases (63.9 kg) but less than that of the remaining cohort members who never reported a hip fracture (69.3 kg).

The association between protein intake, source, and quality and the risk of hip fracture should be investigated in other populations that include older participants, men, and more dietary diversity. The risk of hip fracture greatly accelerates beyond 70 y of age, the maximum age at baseline in the Iowa study. Our findings of an association between increased dietary protein intake and reduced risk of hip fracture are important because modification of protein intake late in life may be a means of reducing the burden of hip fracture in the elderly.

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