Utah State University [DigitalCommons@USU](https://digitalcommons.usu.edu/)

[All Graduate Theses and Dissertations](https://digitalcommons.usu.edu/etd) [Graduate Studies](https://digitalcommons.usu.edu/gradstudies) Graduate Studies

5-2002

Dietary Protein Intake as Measured by a Picture-Sort Food Frequency Questionnaire and Risk of Osteoporotic Hip Fracture in Aging Residents of Utah

Heidi Jensen Wengreen Utah State University

Follow this and additional works at: [https://digitalcommons.usu.edu/etd](https://digitalcommons.usu.edu/etd?utm_source=digitalcommons.usu.edu%2Fetd%2F5497&utm_medium=PDF&utm_campaign=PDFCoverPages)

P Part of the [Nutrition Commons](http://network.bepress.com/hgg/discipline/95?utm_source=digitalcommons.usu.edu%2Fetd%2F5497&utm_medium=PDF&utm_campaign=PDFCoverPages), and the [Physiology Commons](http://network.bepress.com/hgg/discipline/69?utm_source=digitalcommons.usu.edu%2Fetd%2F5497&utm_medium=PDF&utm_campaign=PDFCoverPages)

Recommended Citation

Wengreen, Heidi Jensen, "Dietary Protein Intake as Measured by a Picture-Sort Food Frequency Questionnaire and Risk of Osteoporotic Hip Fracture in Aging Residents of Utah" (2002). All Graduate Theses and Dissertations. 5497.

[https://digitalcommons.usu.edu/etd/5497](https://digitalcommons.usu.edu/etd/5497?utm_source=digitalcommons.usu.edu%2Fetd%2F5497&utm_medium=PDF&utm_campaign=PDFCoverPages)

This Dissertation is brought to you for free and open access by the Graduate Studies at DigitalCommons@USU. It has been accepted for inclusion in All Graduate Theses and Dissertations by an authorized administrator of DigitalCommons@USU. For more information, please contact [digitalcommons@usu.edu.](mailto:digitalcommons@usu.edu)

DIETARY PROTEIN INTAKE AS MEASURED BY A PICTURE-SORT FOOD FREQUENCY QUESTIONNAIRE AND RISK OF OSTEOPOROTIC HIP FRACTURE IN AGING RESIDENTS OF UTAH

by

Heidi Jensen Wengreen

A dissertation submitted in partial fulfillment of the requirements for the degree

of

DOCTOR OF PHILOSOPHY

m

Nutrition and Food Sciences

Approved:

UTAH STATE UNIVERSITY Logan, Utah

Copyright© Heidi Jensen Wengreen 2002

All Rights Reserved

ABSTRACT

Dietary Protein Intake as Measured by a Picture-Sort Food Frequency

Questionnaire and Risk of Osteoporotic Hip Fracture in

Aging Residents of Utah

by

Heidi Jensen Wengreen, Doctor of Philosophy

Utah State University, 2002

Major Professor: Dr. Ronald G. Munger Department: Nutrition and Food Sciences

Protein is an important component of bone, but the role of dietary protein intake in osteoporosis remains controversial. The Utah picture-sort food frequency questionnaire was found to produce a useful estimation of usual dietary intake in the elderly. This method of dietary assessment was used in a population-based case-control study to examine the relationship between protein intake and risk of osteoporotic hip fracture in elderly Utah residents. Analyses of risk of hip fracture across increasing quartiles of protein intake were stratified by age-group. Higher protein intake was associated with a reduced risk of hip fracture in men and women aged 50-69 years but did not appear to increase or decrease risk of hip fracture in those aged 70-89 years. The relationship appeared to be modified by age. Modification of protein intake late in life may be a useful means to prevent hip fractures in the elderly.

iii

(198 pages)

ACKNOWLEDGMENTS

I wish to extend heartfelt thanks and gratitude to my major professor and mentor, Dr. Ronald G. Munger. Without his invaluable guidance, assistance, and support, completion of this dissertation would not have been possible. I would also like to thank others on my committee, including Drs. Richard Cutler and Chris Corcoran, for their superior statistical advice and assistance, as well as Drs. Deborah Gustafson, Nedra Christianson, and Georgia Lauritzen for their vast knowledge and understanding of human nutrition.

I am also greatly indebted to Ms. Nancy West and Dr. Nancy Sassano as well as to the many interviewers, data coders, and other staff members of the Utah Study of Nutrition and Bone Health for their help in gathering, organizing, and cleaning data used in the analyses of this project.

I thank my parents for their unconditional love and encouragement. They taught me by example that through hard work and dedication, goals can be accomplished.

Finally, I am grateful beyond words for my husband, Clay, who without question has sustained my educational pursuits both emotionally and financially . His continuous love and support have been and will continue to be the motivating force behind any success I may claim as a researcher.

The research presented in this publication was sponsored by grant ROl AR43391 from the U.S. National Institute of Arthritis and Musculoskeletal and Skin Diseases (Dr. R.G. Munger, P.I.), and funding from the Agricultural Experiment Station and the Office of the Vice-President for Research of Utah State University.

 iv

CONTENTS

 $\bar{\mathbf{V}}$

AP

LIST OF TABLES

LIST OF FIGURES

 ix

CHAPTER 1

INTRODUCTION AND BACKGROUND

Abstract

Osteoporosis and related bone fractures are major health concerns for aging populations worldwide. Hip fractures are the most clinically serious of all fractures associated with osteoporosis. Protein is important to bone health but it is unknown whether optimal dietary protein intake may prevent the incidence of hip fracture. A population-based case-control study of elderly men and women in Utah was conducted to examine the relationship between dietary protein intake and other dietary and genetic factors and risk of hip fracture. Careful consideration of age-related limitations of the study population led researchers to design a picture-sort food frequency questionnaire (FFQ) as the method of dietary assessment. The two-step picture-sort FFQ was intended to estimate usual dietary intakes of respondents who may have physical and cognitive limitations associated with aging. A substudy designed to examine the validity and reproducibility of the picture-sort FFQ method was conducted. Strengths, limitations, and methodologic aspects of food-frequency questionnaires in general and the picturesort FFQ in specific are reviewed.

Introduction

Osteoporosis is a major health concern for the elderly in North America and Europe and is an emerging problem for the elderly of developing countries. Defined as a condition of low bone mass, microarchitectural deterioration of bone tissue, and

increased bone fragility, osteoporosis often results in fractures of the forearm, spine, or hip (1). Hip fractures are the most serious of all osteoporotic fractures and cause excess mortality and morbidity, decreasing length and quality of life for millions of elders worldwide (2). The annual cost of treating osteoporotic hip fracture in the U.S. alone is estimated at 10 - 20 billion dollars and is expected to rise exponentially as the population ages (2). Careful examination of risk factors associated with this condition may lead to important new prevention and treatment strategies to decrease the already enormous burden and cost associated with outcomes related to osteoporosis.

Pathologically osteoporosis may result from inadequate peak bone mass, excessive bone resorption, or impaired bone formation, each important during different stages of the lifecycle (3). In addition, fracture risk involves factors that affect the incidence and severity of falls. Several genetic and environmental risk factors for osteoporosis and related fractures have been identified. Nutritional factors are among the most important modifiable factors in the development and maintenance of bone mass and strength, and thus the prevention of fractures.

Dietary interventions for the prevention and treatment of osteoporosis have long been focused on calcium, phosphorous, and vitamin D. The mineral content of bone is roughly 80 - 90% calcium and phosphorous; thus, dietary deficiencies of either result in reduced bone mineral density (4). Vitamin D influences calcium and phosphorous metabolism and balance through influences on the bone as well as the intestine and kidney (4). Although less well studied, other nutrients are also crucial to the formation, mineralization, and metabolism of bone tissue and may have important implications in prevention and treatment strategies. Protein, for example, is an important component of the bone matrix but until recently has not been implicated as a potential risk factor for osteoporotic fracture.

Several lines of evidence point to a role for dietary protein intake in bone health, but the relationship between dietary protein and risk of osteoporotic fracture is unclear. Malnutrition, especially protein-energy malnutrition, is often observed in the elderly and appears to be more severe in patients with hip fracture than in the general aging population (1). Less than optimal dietary protein intake may contribute to both the occurrence and complications of osteoporotic hip fractures in at-risk populations. Protein supplementation improves medical outcomes of elderly hip fracture patients (5-7), but it is unclear whether optimal dietary protein intake may prevent the incidence of hip fracture. Although several population-based observational studies have examined the relationship between dietary protein intake and risk of hip fracture, their results are conflicting (8-11). Additional details surrounding the controversy of protein's role in bone health and risk of hip fracture are described in Chapter 3.

A population-based case-control study of elderly men and women in Utah, the Utah Study of Nutrition and Bone Health (USNBH), was designed to further examine the relationships between dietary protein intake and other nutrition and genetic factors and risk of hip fracture. The elderly population of Utah was well suited to examine these relationships due to low rates of co-morbidity, high rates of participation in observational studies, and high median life expectancy (12-13). The average age of men and women aged 50- 89 years who agreed to participate in the USNBH was 75.4 years, most were Caucasian (96.8%), and a large percentage had at least a high school education (84.1%).

Other demographic characteristics of participants in the USNBH may be found in Appendix A.

Rates of hip fracture increase exponentially with age for both men and women, so many study participants were expected to be of advanced age. Furthermore, cases with recent hip fracture were expected to be frailer than participants of the same age without hip fracture. Cognitive and physical limitations commonly associated with aging, such as difficulties in seeing, hearing, and remembering, were carefully considered when methods for collecting dietary, medical, and demographic data were designed. The USNBH interview included detailed information on recent and past histories of physical activity, supplement use, medication use and medical conditions, bone fractures and falls, alcohol and tobacco use, weight and height, occupations, reproductive history, and estrogen use in women, as well as a family history of falls and fracture. The USNBH interview booklet may be found as Appendix B.

One of the first methodologic decisions of any population-based observational study examining diet-disease relationships is the selection of an appropriate dietary assessment method. Methods of dietary assessment commonly used in large-scale observational studies to give a measure of usual dietary intake include multiple shortterm dietary recalls, diet histories, food frequency questionnaire, and biochemical indicators of specific nutrients (14). Selection of a dietary assessment method depends on the limitations of time, budget, the motivation of participants, and interviewer effort.

The Utah picture-sort food frequency questionnaire (FFQ) was the dietary assessment method used in the USNBH. The Utah picture-sort FFQ was developed

specifically for the elderly Utah population as an alternative to the more traditional paperand-pencil format FFQ. A substudy testing the validity and reproducibility of the Utah picture-sort FFQ was conducted in a sample of randomly selected controls from the USNBH population (Chapter 2). The usual dietary intakes from the average of three multiple 24-hour recalls were compared to usual dietary intake from two administrations of the picture-sort FFQ. This validity and reproducibility study was necessary to assess the performance of the dietary assessment method and the precision to which it would rank usual dietary intake and identify differences between extremes in dietary intakes. Information on the selection of this method and the importance of assessing its validity and reproducibility follow in the background section of this chapter. The picture-sort FFQ form may be found as Appendix C.

Background

The food frequency questionnaire is often the dietary assessment method of choice in large-scale epidemiological research to study relationships between diet and disease. The food frequency method of dietary assessment consists of a list of food items for which respondents report frequency of consumption in a specified period in the past. Development of this method for dietary assessment began in the 1950s by Stephanik and Trulson, Heady, and Marr and others (14). Using diet records collected by British bank clerks, Heady demonstrated that the frequency of food usage correlated highly with the total weights of the same foods consumed over a period of several days (14).

In general, feasibility and budget considerations are among reasons investigators select the FFQ method for use in large studies, but the FFQ is superior to other methods

in other important aspects (15). First, the food frequency questionnaire is designed to estimate and rank respondents' usual food intake (16). Because of intra-individual variability in diet, other methods of assessing usual intake would require collection of large numbers of 24-hour recalls or diet records that require much more time and money (15). Second, in food frequency questionnaires respondents are usually asked to simply report frequency of consumption of a list of food items. These questionnaires can be easily self-administered in a relatively short amount of time, making the dietary data less burdensome and less expensive to collect (15). Third, the food frequency questionnaire is the only method able to measure usual intake in the remote or recent past in a single administration (15).

Despite its many strengths, the FFQ method has limitations. The FFQ method sacrifices precision in intake estimates because it measures usual intake over an extended period of time in one administration (14). Many details of dietary intake are not measured and quantification of intake is not as accurate as dietary recalls or records (16). FFQs usually do not collect information for specific food items. Foods are typically grouped into broad categories and the nutrient value is estimated as an average for all foods in that group or assigned from the value of one food representing the entire group (17). Errors in reporting or assuming a standard serving size for groups of foods may influence nutrient intake estimates considerably (16). In addition, overestimation of total nutrient intake with longer food lists and underestimation with shorter food lists may not be identified if the true distribution of intakes for the population under study is unknown (16).

As with any research instrument, it is important to evaluate the method's ability to provide valid and reliable data in the population of study before such data are used in analyses of the study objectives. Even small changes in the method's design may affect performance, so each dietary assessment instrument should be evaluated for reliability and validity in the population for which it was designed (14) (18). The reliability of a method is a measure of the ability of that method to provide consistent results when applied to the same subjects on several occasions. Validity refers to accuracy and describes how well a method or instrument measures what it was designed to measure (19). Reliability is not the same as validity; a method may be reliable without being valid.

The Utah Hip Fracture picture-sort FFQ was designed to rank individual intakes of selected nutrients in a population of elderly people in Utah who are 50 years of age or older. This method, known as the picture-sort FFQ, uses a two-step, partly selfadministered picture-sort format to present the food list and obtain frequency of food consumption and was first developed by Shiriki Kumanyika for use in the Cardiovascular Health Study (20).

The picture-sort FFQ method as used in the Cardiovascular Health Study was validated using one administration of the picture-sort FFQ and six 24-hour recall dietary interviews. Comparisons and correlations of nutrient intakes estimated by the picturesort FFQ and the averaged 24-hour recalls were used for analysis. Adjusted Pearson correlation coefficients from the data ranged from 0.41 - 0.74 for macronutrients and 0.26 - 0.62 for micronutrients (20-21). It was concluded that the picture-sort method of administering a food frequency questionnaire gave estimates of mean nutrient intakes

comparable with estimates based on 24-hour recalls, and correlations with reference data were similar to those reported in literature for conventionally administered paper-andpencil food frequency questionnaires.

Kumanyika et al. (20-21), suggested that structuring the food frequency reporting technique as a picture-sort may improve ease of response without compromising data quality. The picture sort method may permit better identification of foods by persons with impaired vision or poor reading skills as frequently encountered when studying elderly populations. Because the literacy demand on the respondents is small, this method may be used on respondents with different reading levels. Including respondents of all different reading levels in the study, instead of excluding those who cannot read the directions or food list, may help ensure that the study population represents the actual population of interest. Having the respondents sort and then review the cards a second time before reporting frequency may increase respondents' cognitive orientation to food recall and help them to give more accurate descriptions of consumption frequencies.

Validation of a diet assessment tool involves the comparison of results obtained from a test method, here the picture-sort FFQ, to results obtained from an alternative method of dietary assessment with proven validity. In previous food frequency validation studies, multiple 24-hour recalls, weighed diet records, and diet histories have been used as the "gold standard" of dietary assessment, although none is a perfect comparison model for actual usual dietary intake. As reported in the literature, correlations among the estimated mean nutrient intakes measured from food frequency methods and standard dietary assessment methods, including 24-hour recalls, weighed diet record, and diet histories, commonly range from 0.3- 0.7 (22). Correlations among

repeat assessments using a food frequency questionnaire are generally higher (0.50- 0.80) (22). Even though these correlations may seem somewhat low, they are within the range of validity and repeatability of other biological measures such as blood pressure or skinfold measurements and are interpreted to be acceptable for determining validity and reliability (23).

Among the comparison methods for validating a FFQ, diet records are a likely gold standard (14). Diet records are open-ended, do not depend on memory of the respondent for accuracy, and allow for direct assessment of portion sizes by measurement of weight, volume, or dimensions. However, many days of diet records are needed to represent usual intake of the individual. Pietinen et al. designed a food frequency questionnaire to estimate usual intake of selected foods among 217 middle-aged men in Finland and found that a food record covering seven to 14 nonconsecutive days is necessary to classify usual intake (19). Willett (14) also found that correlations between FFQs and food record data were highest with four, seven-day records versus correlation from one, two, or three, seven-day records. Findings from both reports suggest that longer observation periods for the food records are needed to assess usual intake. However, because of respondent burden and extreme costs associated with collecting many days of diet records, this method is infeasible for many large validation studies.

The primary alternative to the use of diet records in validating FFQs is the collection of multiple 24-hour recalls (14). Using the 24-hour recall method, the respondent is asked to remember and report all the foods and beverages consumed during the preceding day. By collecting multiple 24-hour recalls at intervals of approximately three months on different days of the week, it is possible to obtain a representation of

long-term average intake correcting for seasonal and day-to-day variations in individuals' diets. An innate weakness in the 24-hour recall is respondent error in reporting the previous day's consumption. As mentioned previously, the marked decline in short-term memory with age makes the 24-hour recall in the elderly particularly difficult (24). However, the 24-hour recall takes approximately 20 minutes to complete and can be administered over the telephone by a trained interviewer (16). Because the 24-hour recall causes little respondent burden, those willing to complete 24-hour recalls may be more representative of the population than those willing to do extensive diet recording. Reported correlations between 24-hour recalls administered by telephone and in-person interview on different days range from 0.43 to 0.84 (25).

In validation studies of FFQs it is important to account for factors in the design of the study that may affect correlation coefficients between the test and gold-standard methods that may lead to false conclusions. Factors to consider include, but are not limited to, the sequence of administration of the test and gold-standard assessment methods, the need to adjust nutrient intake scores for total energy intake to correct for over- or underestimation of intake, the inclusion or exclusion of portion sizes in the food frequency questionnaire, and the need to analyze the data by gender and age categories.

The sequence of administration of the test and gold-standard dietary assessment is very important. Ideally, the questionnaire being validated should be administered prior to the assessment of the gold standard for two reasons. First, if the validation study is a substudy of a larger study, subjects for whom the validated method is to be used will encounter the food frequency questionnaire independent of any other dietary assessment (26). The validation study should mimic this sequence. Second, the completion of one

method might affect the performance of the other method by drawing respondents' attention to their diets (27).

Willett et al. (27) studied these issues in a validation study of a 61-item semiquantitative FFQ used in a large prospective study among women. Study participants were asked to record a weighed inventory of their diet for one week, four times during the year. These data were then compared with the test method administered once at the beginning and once at the end of the study (27). Results of the second versus the first FFQ correlated better with the diet records. Correlations ranged from 0.33 for protein to 0. 73 for vitamin C for the second administration, compared with 0.18 - 0.53 for the first administration. These results suggest that increased awareness of diet may have influenced the second set of responses. If the test method must be administered after the standard method to meet study objectives, it is suggested that researchers wait 3 to 4 weeks to administer the test method to help minimize the effects of increased awareness of diet (26).

Another factor of concern in food frequency validation studies is the tendency for FFQs to overestimate or underestimate average nutrient intakes. Feskanich et al. (8) reported that in a validation study of a 131-item semi-quantitative food frequency questionnaire, 127 male participants overestimated their usual consumption of foods perceived as healthy while underreported their consumption of foods considered to be less healthy. It was found that dairy food and the food group containing eggs, meat, and fish were slightly underestimated and that fruits and vegetables were grossly overestimated by a mean of 85% and 102%, respectively.

Data from the third National Health and Nutrition Examination Survey (NHANES III) support the observed trend of underreporting energy intake in population reference data. The primary dietary assessment instrument used in NHANES III was the 24-hour recall. Underreporting was assessed by computing a ratio of energy intake to estimated basal metabolic rate for each participant and then comparing to a population standard (28). Additional data support the survey's findings that 18% of men and 28% of women were classified as underreporting energy intake (28). In a study of persons aged 56 - 81 years, underreporting was found to be higher in women and was associated with adiposity in older women but not in older men (29).

NHANES III data also suggest that intakes vary according to the day of the week, with underreporting being greater for nonweekend days. Mean energy intake was higher in men on Saturday and Sunday and in women on Friday and Saturday (28). Other findings showed that the mean numbers of meals, snacks, and foods were lower in underreporters than in those reporting adequate energy intake. This suggests that omitted foods, meals, and snacks, rather than differences in portion size, may account for the lower reported intakes (28).

To account for errors in over- or underreporting of total energy intake, Willett et al. (27) recommended nutrient intake scores be adjusted for total energy intake. Energyadjusted correlation coefficients tend to be higher than crude correlation coefficients because nutrient intakes are better estimated as a proportion rather than an absolute amount. In the method reported, residuals from regression models are computed with total caloric intake as the independent variable and the nutrient intake score as the dependent variable. Residuals are then added to the expected nutrient value for the mean

caloric intake of the specific age and gender group of participant in the study population to obtain a score adjusted to the average caloric intake (27). As was previously mentioned, correlation coefficients tend to be higher for calorie-adjusted intakes than for absolute intakes. In Willett's data, unadjusted correlation coefficients ranged from 0.26 for total vitamin A without supplements to 0.73 for Vitamin C and adjusted correlation coefficients ranged from $0.36 - 0.75$ (27). These results are consistent with findings from other researchers. In a study comparing a FFQ and diet history questionnaire to a 7 -day food record, Jain et al. (30) reported unadjusted correlation coefficients in Toronto, Canada men from 0.17 for thiamin to 0.70 for calcium and adjusted correlation coefficients from 0.26- 0.72.

The importance of collecting data about portion size in addition to the estimation ofFFQ consumption remains controversial. Results from some studies suggest additional questions about serving size do not appreciably increase correlations between FFQs and diet records or recalls. Hankin et al. reported a slight increase in correlation with data on portion size from 0.55 - 0.59 (31). In other studies, as summarized by Willett, similar small increases were observed from correlations of $0.32 - 0.37$, $0.41 - 0.43$, $0.49 - 0.54$, and 0.50- 0.50 (31). It is apparent that the data collected during the interview on portion size added little to the assessment of nutrient intake in these studies. From historical research we know that frequency explains most of the variation in total amount of a food consumed, and that the within-person variation in serving size for nearly all foods is much greater than the between-person variation in serving size (16) (31). Among a total of 66 foods examined by Hunter et al., the average ratio of within-person variation to

between-person variation was approximately 4 (16). Large within-person variation on usual amounts of foods eaten makes it difficult to assign a usual portion size.

When necessary for quantification of usual nutrient intake, either the investigator or the participant may specify usual portion size. If specified by the investigator, the frequency is asked in terms of a specified portion size; if specified by the participant, usual portion size is stated for each food in addition to frequency of consumption (32). Whether the subject or the investigator specifies the portion size, the problem remains that portion sizes for individual foods are condensed into average portion sizes for a category of foods. Advantages to investigator-specified portion sizes are decreased time, effort, and cost needed to collect and enter dietary data. Individual report of usual portion size of each consumed food is unlikely to substantially improve the accuracy of the FFQ method (14).

Because men and women may respond to questionnaires differently, validation studies that include both men and women must be analyzed separately (26). If both genders are analyzed together, correlation coefficients will not represent the relation between the test method and the gold standard of the two subsets of the population. This is illustrated by differences in mean zinc intake as estimated by a FFQ compared to a 16 day weighted inventory in 24 men and 28 women aged 25 - 64 years (26). The correlation coefficient between the two methods for the entire study population was 0.43. When data were analyzed separately by gender, correlation coefficients were 0.69 for women and 0.33 for men.

The FFQ method for assessing diet has many advantages including low cost of administration, modest demand on participants, and documented validity of measuring

long-term diet. For these reasons and others it is more commonly the dietary assessment method of choice in large case-control and cohort studies with increasing use in clinical research and practice.

Although many improvements have been made in the FFQ method in the past decade, FFQs are still far from perfect. Researchers should continue to improve precision and accuracy in this method by conducting reproducibility and validity studies to assure accurate measures of diet-disease relationships. Accuracy may be improved by adding additional food items to the questionnaire, collecting detail on portion size, adding additional open-ended responses to report foods usually eaten but not included in the food list, and capturing important information on food preparation methods (31). However, the added time, cost, and respondent burden induced by the addition of these and other factors must be weighed against the gained information and improvements in accuracy of information. According to Willett (31), future improvements should focus on conducting validation studies in diverse populations of age and culture, including additional biochemical comparisons, and making changes in the questionnaire as the diet of the population under study changes.

Project Objectives

- I. To evaluate the Utah picture-sort food frequency questionnaire for the measurement of usual dietary intake of elderly study participants, examining differences by age and gender.
- 2. To examine associations between total, animal, and vegetable protein intake and risk of hip fracture in aging residents of Utah.

References

1. Bonjour JP, Schurch MA, Rizzoli R. Nutritional aspects of hip fractures. Bone 1996; 18: 139S-144S.

2. Heaney RP. Nutritional factors in osteoporosis. Annu Rev Nutr 1993;13 :287-316.

3. Raisz LG, Prestwood KM. Epidemiology and pathogenesis of osteoporosis. Clinical Cornerstone 2000;2: 1-10.

4. Ilich JZ, Kerstetter JE. Nutrition in bone health revisited: a story beyond calcium. JAm Coli Nutr 2000; I9:7I5-37.

5. Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. Dietary supplementation in elderly patients with fractured neck of the femur. Lancet 1990;335:1013-6.

6. Schurch MA, Rizzoli R, Slosman D, Vadas L, Vergnaud P, Bonjour JP. Protein supplements increase serum insulin-like growth factor-I levels and attenuate proximal femur bone loss in patients with recent hip fracture . A randomized, double-blind, placebo-controlled trial. Ann Intern Med I998;128:80I-9.

7. Tkatch L, Rapin CH, Rizzoli R, et al. Benefits of oral protein supplementation in elderly patients with fracture of the proximal femur. J Am Coll Nutr 1992;11:519-25.

8. Feskanich D, Willett WC, Stampfer MJ, Colditz GA. Protein consumption and bone fractures in women. Am J Epidemiol I996;143 :472-9.

9. Munger RG, Cerhan JR, Chiu BC. Prospective study of dietary protein intake and risk of hip fracture in postmenopausal women. Am J Clin Nutr I999;69:I47-52.

10. Hannan MT, Tucker KL, Dawson-Hughes B, Cupples LA, Felson DT, Kiel DP. Effect of dietary protein on bone loss in elderly men and women: the Framingham Osteoporosis Study. J Bone Miner Res 2000; 15:2504-12.

11. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Am J Clin Nutr 2001;73:118-22.

12. Slattery ML, French TK, Egger MJ, Lyon JL. Diet and survival of patients with colon cancer in Utah: is there an association? Int J Epidemiol 1989; 18:792-7.

13. Kranczer S. Changes in longevity by state. Stat Bull Metrop Insur Co 1998;79:29- 36.

14. Willett WC. Nutritional epidemiology. New York: Oxford Press, 1990.

15. Liu K. Statistical issues related to semiquantitative food-frequency questionnaires. Am J Clin Nutr 1994;59:262S-265S.

16. Thompson FE. Dietary assessment resource manual. Journal of Nutrition 1994; 124:2247s-2249s.

17. Briefel RR, Flegal KM, Winn DM, Loria CM, Johnson CL, Sempos CT. Assessing the nation's diet: limitations of the food frequency questionnaire. J Am Diet Assoc 1992;92:959-62.

18. Coates RJ, Monteilh CP. Assessments of food-frequency questionnaires in minority populations. Am J Clin Nutr 1997;65:1108S-1115S.

19. Zulkifli SN, Yu SM. The food frequency method for dietary assessment. JAm Diet Assoc 1992;92:681-5.

20. Kumanyika S, Tell GS, Fried L, Martel JK, Chinchilli VM. Picture-sort method for administering a food frequency questionnaire to older adults. J Am Diet Assoc 1996;96:137-44.

21 . Kumanyika SK, Tell GS, Shemanski L, Martel J, Chinchilli VM. Dietary assessment using a picture-sort approach. Am J Clin Nutr 1997;65: 1123S-1129S.

22. Freedman LS, Carroll RJ, WaxY. Estimating the relation between dietary intake obtained from a food frequency questionnaire and true average intake. Am J Epidemiol 1991;134:310-20.

23. Kushi LH. Gaps in epidemiologic research methods: design considerations for studies that use food-frequency questionnaires. Am J Clin Nutr 1994;59: 180S-184S.

24. Van Staveren WA, De Groot LC, Blauw YH, Vander Wielen RP. Assessing diets of elderly people: problems and approaches. Am J Clin Nutr 1994;59:221 S-223S.

25. Lyu LC, Hankin JH, Liu LQ. Telephone vs face-to-face interviews for quantitative food frequency assessment. JAm Diet Assoc 1998;98:44-8.

26. Margetts BM. Design concepts in nutritional epidemiology. New York: Oxford Press, 1991.

27. Willett WC, Sampson L, Stampfer MJ. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985; 122:51-65.

28. Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. Dietary methods research in the third National Health and Nutrition Examination Survey: underreporting of energy intake. Am J Clin Nutr 1997;65:1203S-1209S.

29. Johnson RK, Goran Ml, Poehlman ET. Correlates of over- and underreporting of energy intake in healthy older men and women. Am J Clin Nutr 1994;59:1286-90.

30. Jain M, Howe GR, Rohan T. Dietary assessment in epidemiology: comparison on food frequency and a diet history questionnaire with a 7-day food record. Am J Epidemiol 1996; 143:953-60.

31. Willett WC. Future directions in the development of food-frequency questionnaires. Am J Clin Nutr 1994;59:171S-174S.

32. Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, Willett WC. Variability in portion sizes of commonly consumed foods among a population of women in the United States. Am J Epidemiol 1988;127:1240-9.

CHAPTER 2

COMPARISON OF A PICTURE-SORT FOOD FREQUENCY QUESTIONNAIRE WITH 24-HOUR DIETARY RECALLS IN AN ELDERLY UTAH POPULATION¹²

Abstract

Objective: To evaluate the 137-item Utah picture-sort food frequency questionnaire (FFQ) in the measurement of usual dietary intake of older adults.

Design: The picture-sort FFQ was administered at baseline and again one year later. Three seasonal 24-hour dietary recall interviews were collected during the year between the two FFQs. Mean nutrient intakes were compared between methods and between administrations of the FFQ.

Setting: The FFQ interviewers were administered in respondents' homes or care-centers. The 24-hour diet recalls were conducted by telephone interview.

Subjects: Two-hundred eight men and women ages 55- 84 years were recruited by drawing a random sample of controls from a case-control study of nutrition and bone health in Utah.

Results: After adjustment for total energy intake, median Spearman rank correlation coefficients between the two picture-sort FFQs were 0.69 for men aged ≤ 69 years, 0.66 for men aged > 69 years; 0.68 for women aged ≤ 69 years, and 0.67 for women aged $>$ 69 years. Median correlation coefficients between methods were 0.50 for men ≤ 69 , 0.52 for men > 69 ; 0.55 for women ≤ 69 , and 0.46 for women > 69 .

¹Coauthored by Heidi J. Wengreen, Ronald G. Munger, Siew Sun Wong, Nancy A. West, and D. Richard Cutler.

² Published in Public Health Nutrition, 2001; 4, 961-970. Copyright retained by the authors.

Conclusions: We report intake correlations between methods and administrations comparable to those reported in the literature for traditional paper-pencil FFQs and to one other picture-sort method of FFQ. This dietary assessment method may improve ease and accuracy of response in this and other populations with low literacy levels, poor memory skill, impaired hearing, or poor vision.

Introduction

Food-frequency questionnaires (FFQ) are commonly used in epidemiologic research on diet and disease to rank individuals according to usual nutrient intake 1. Customarily, using a paper-and-pencil FFQ respondents are asked to report frequency of consumption for a list of foods 2. However, low literacy levels along with common cognitive and physical limitations, such as poor memory and impaired vision and hearing, are often encountered when studying elderly populations and may limit the use of traditional FFOs in this population 3 . Kumanyika et al. 4 developed a picture-sort method of administering a food frequency questionnaire that may help to improve accuracy of response in elderly populations by easing respondent burden. We constructed a picture-sort FFQ, based on the method developed by Kumanyika, for use in the Utah Study of Nutrition and Bone Health (USNBH), a large statewide case-control study of the determinants of hip fracture in elderly Utah residents.

The aim of this study was to evaluate the 137-item Utah picture-sort FFQ in the measurement of usual dietary intake in older adults. We tested relative validity of the Utah picture-sort FFQ by comparing nutrient intakes reported from the FFQ to a measure of usual dietary intake. Although dietary recalls and FFQs, both self-report methods, are

likely to have some degree of correlated error, we used the average of three 24-hour dietary recall interviews, collected by telephone interview using a multiple pass format, as a measure of usual dietary intake. This method seemed like a reasonable option to the more widely used but burdensome dietary records especially when considering the elderly population of interest in which we may encounter poor literacy skills or low motivation. To test reproducibility of the method we compared reported nutrient intakes from two administrations of the picture-sort FFQ taken one year apart.

Although the FFQ has been widely used in diverse populations of middle-aged adults, its use in the elderly, especially in respondents over the age of 70 years, is relatively unexplored 5-7. We examined differences in reports of nutrient intakes using the picture-sort FFQ between younger and older elderly participants by comparing agreement between nutrient estimates made from the test and reference method by gender and age strata (men and women ≤ 69 years of age, men and women > 69 years of age).

Materials and Methods

Subjects and Design

The Utah Picture-Sort FFQ was developed for use in the USNBH study, which includes Utah residents with and without hip fractures ages 50 to 89 years. Participants in the dietary assessment study were selected from controls of the USNBH study and were invited to participate in the dietary study after completion of the USNBH baseline interview.

Respondents completed two picture-sort FFQ interviews and three 24-hour dietary recall interviews over the course of approximately one year. Respondents began

the study by completing their first FFQ between March 1998 and March 1999 (Figure 2- 1) at the time of their baseline interview for the USNBH. The three 24-hour dietary recall interviews were collected during the year between the first administration of the FFQ and the second administration of the FFQ. During the FFQ interview, the respondent was asked to report frequency of consumption of selected foods during the previous year. Because of this reference time, the second FFQ was expected to give a measure of usual dietary intake in the same period of time the three 24-hour recalls were collected.

The picture-sort FFQs were administered in the home of each respondent by a trained interviewer and lasted approximately 35 minutes. Trained interviewers also administered the multiple-pass 24-hour dietary recall interviews by telephone. The telephone 24-hour recall interviews lasted approximately 25 minutes.

Picture-Sort Food Frequency Questionnaire

The Utah picture-sort FFQ food list includes 137 food cards containing one or more food items that were systematically selected from the 126-item Nurses' Health Study (NHS) FFQ 8, the National Cancer Institute (NCI) FFQ 9, and a list of commonly eaten foods as identified in focus groups. A modified version of the 126-item Nurses Health Study FFQ used in the Iowa Women's Health Study was administered to approximately 4500 persons in Cache Valley of Northern Utah. Food items that contributed less than 1.0% of total mean intake and had an R^2 factor less than 0.01 of each of 25 key nutrients, indicating that a food item explained less than 1% of the variation in intake of 25 key nutrients, were dropped from the subsequent list. This list

Figure 2-1 Sequence of dietary interviews of controls from the Utah Study of Nutrition and Bone Health who participated in the follow-up dietary assessment study; March 1998 to April 2000.

was then merged with the NCI FFQ food list and a list of commonly eaten foods as identified from focus groups. The final food list includes nearly all items from the NCI list and the NHS list but in slightly different categories that may be more inclusive or more specific than in other dietary assessment tools.

The picture-sort FFQ method, first developed by Kumanyika for use in the Cardiovascular Health Study 4 , 10 , is an adaptation of a written FFO that engages respondents by having them sort color picture cards into trays representing frequency of use. The Utah picture-sort FFQ cards developed at Utah State University were laminated 4-inch x 6-inch cards with color photographs of one or more food items. For ease in respondent sorting, the cards were separated into seven categories: 1) beverages, 2) fruits, 3) vegetables, 4) dairy products, 5) meats, fish egg, and main dishes, 6) cereals and breads, and 7) snacks, and oils and other foods. In most cases the picture card depicted a standard size portion of the food or foods placed on a 1 0-inch dinner plate, in a 6-inch cereal bowl, or in a 12-ounce glass. Standard portion sizes were also listed on the reverse side of the card in common household measures (1 cup, 1 medium piece, etc.) for interviewer reference.

Following the picture-sort method as described by Kumanyika, each respondent was given categories of picture-cards one at a time and asked to sort them into five trays according to period of use (i.e., daily, weekly, monthly, yearly, or rarely/never) over the past year. After all categories of picture cards were sorted, respondents were asked about specific frequency of use for food items placed in the trays starting with the daily tray and proceeding to the rarely/never tray.

We did not ascertain information about vitamin and mineral supplement intake as part of the picture-sort FFQ method. The Utah picture-sort FFQ was designed to ascertain information about the frequency of consumption of a list of foods only. In practice, the picture-sort should be combined with additional questions about the use of nutritional supplements, food preparation, and other additional questions that may be pertinent to the research questions.

24-Hour Recalls

The three 24-hour dietary recall interviews were administered approximately three months apart during the year between the two FFQ interviews to capture seasonal differences in intake. All 24-hour recalls were administered on random days of the week and included at least one weekend day (Saturday or Sunday). A two-dimensional representation of the National Health and Nutrition Examination Survey threedimensional food models 11 was mailed to respondents before their first interview. Participants were instructed to keep the guide near their telephone for use in the interviews. Telephone interviewers used an adaptation to the multiple-pass dietary recall collection method originally developed by the US Department of Agriculture (USDA)- Human Nutrition Information Service (HNIS) 12 to obtain information about a respondent's food intake during the preceding day. Interviewers were trained to probe for detailed and accurate information on food preparation, food type, and portion size for each food reported during the recall interview.

Dietary recall interviews were edited for completeness, coded, and entered into the Food Processor dietary assessment program (Version 7.1, Food Processor Nutrition
Analysis & Fitness Software, Version 7.1 , ESHA Research, Salem, Oregon). The Food Processor program contained nutrient data from USDA as well as additional sources. Mean individual nutrient intakes were calculated from the average of the three dietaryrecalls. A nutrient database developed for the picture-sort FFQ food list also used the Food Processor program. Food selection for food cards which listed more than one food were made by selecting the most frequently reported food in that category from the coded 24-hour dietary recall interviews. A registered dietitian performed this coding and selection process. FFQ data were converted to mean daily intakes by transforming all consumption periods to consumption per day and then multiplying by frequency of use and weight of the standard serving size.

Statistical Analysis

Means and standard deviations for energy and nutrient intake from food and beverages excluding nutrition supplements estimated by each of the two picture-sort FFQs and by the average of the three 24-hour dietary recalls were calculated. Nutrient intakes were adjusted for total energy intake using the residual method of Willett and Stampfer 13.

Agreement between administrations of the FFQ and between methods was assessed by calculating Spearman rank and Pearson product-moment correlation coefficients between the two picture-sort FFQs for both crude and energy-adjusted nutrient intakes. We report Spearman rank correlation coefficients as they correlate rank order of estimated nutrient intakes between methods and between administrations without assuming a Gaussian distribution for the nutrient intake in the population. Means,

standard deviations, and ratio of means for total energy and nutrient intakes estimated by each of the FFQs and the average of the three-recalls were also calculated. Means were compared by paired t tests.

In evaluation of agreement between methods the second FFQ was compared to the average ofthe three recalls. We used the second FFQ to calculate correlations because this gave a measure of intake from the same period of time the three 24-hour recall interviews were obtained.

To assess variability in daily intake, intraclass correlation coefficients for nutrient estimates from the three 24-hour dietary recall interviews were calculated ^{14, 2}. A oneway random effects analysis of variance model was fit to the data, and the intraclass correlation coefficient was calculated as the ratio of between-subject variance to total variance.

All data were analyzed separately by gender and by the four age-gender strata in Table 2-1. Analyses were performed using SPSS for Windows (version 10, SPSS Inc., Chicago, Illinois).

Results

Ofthose respondents who agreed to participate in the dietary assessment study 217 (75% of both men and women) completed all dietary interviews. Reasons for dropout from the dietary assessment study included refusal, death, severe illness, or interviewer inability to locate respondents. Because participants were selected from a sample of randomly selected controls who previously completed an interview for the

USNBH, they may represent a population of people more willing to participate in health related studies than the general aging population of Utah.

A registered dietitian reviewed the FFQs and 24-hour diet recalls of poor quality identified by comments made by the interviewer at the time of interview. Nine participants (7 men, 2 women) with implausible reported usual energy intake (<500 or >3,500 kcal) by either of the two FFQs or by the average of the 24-hour recalls were excluded from analyses. Characteristics of the remaining 208 participants (103 men, 105 women) are reported in Table 2-1.

Study participants were grouped according to age and gender. The mean age of study participants was 69 years. Participants who were 69 years old or younger at the baseline interview were labeled as younger elderly men or women and those greater then 69 years old at the baseline interview were labeled as older elderly men or women.

Most (>90%) of participants in all age-gender groups were white, not of Hispanic origin, and a high percentage of respondents $(278%)$ in all age gender categories had at least a high school education. Females had higher modified adjusted mini-mental examination scores than males as did younger respondents compared to older respondents. Adjusted mini-mental examination scores ranged from 21 to 30 for all respondents.

Body Mass Index (BMI) based on self-reported heights and weights was similar for both men and women, and older participants had lower BMls compared to younger respondents. Fewer women than men, and fewer older participants than younger participants reported ever regularly or currently smoking cigarettes, or ever regularly or currently drinking alcohol. A greater percentage of women than men, and older women

29

Table 2-1 Selected characteristics of participants in the Utah dietary assessment study; March 1998 to April 2000.

^a Mean value.

^b Standard deviation.

^c Percent of total participants in each subgroup.

than younger women reported currently taking multivitamin mineral supplements or herbal preparations (Table 2-1).

We compared mean energy and nutrient intakes from food and beverages for macronutrient and selected micronutrients from the second FFQ and the average of three 24-hour dietary recalls by age-gender strata (Table 2-2). Mean nutrient intake estimates from our 137 item picture-sort FFQ were generally higher than nutrient intake estimates from traditional and picture-sort FFQs in other elderly populations 10, 15, 16. However, in the studies referred to above, the foodlists were shorter, which may have an influence on the estimated intakes measured from the method. Mean intake estimates from the FFQ were consistently higher than mean intake estimates from the 24-hour dietary recalls; however, the degree of difference varied by age-gender strata. Several investigators have also reported greater mean intakes from FFQs as compared to reference methods 6, 17, 18.

Differences in mean intakes are reported as ratios of mean nutrient intake estimates from the FFQ to nutrient intake estimates from the 24-hour dietary recalls and are included in Table 2-2. The median ratios of mean reported intake were 1.26 in younger men, 1.25 in older men, 1.23 in younger women, and 1.22 in older women.

Mean energy-adjusted nutrient intakes estimated from food and beverages from the first FFQ (administered at baseline) and the second FFQ (administered approximately one year later) were calculated. In general, lower mean energy-adjusted nutrient intakes were estimated by the second FFQ as compared to the first FFQ for all age-gender groups except younger men. Mean energy-adjusted intake estimates for younger men, older men, and older women from the first FFQ and the second FFQ were not significantly

Table 2-2 Means and standard deviations of nutrient intakes estimated from the second administration of the Utah picture-sort food frequency questionnarie and means of three 24-hour dietary recalls by age-gender group; March 1998 to December 1999

^a Ratio of mean FFQ to mean 24-hour dietary recall

b Standard deviation

different from each other for most nutrients. However, in younger women, mean energy-adjusted intake estimates from the first FFQ and the second FFQ were considerably different for most nutrients, and 24 of 28 nutrients tested and I 0 of 13 nutrients shown in Table 2-3 showed statistically significant differences with p-values < 0.05 .

Table 2-3 includes Spearman rank correlation coefficients of selected nutrient intakes estimated from the first FFQ and the second FFQ. Pearson product moment correlations were also calculated, with similar results. Spearman rank correlation coefficients for energy-adjusted nutrients ranged from 0.26- 0.96 for all age-gender groups. Younger men had higher correlations for 9 of 13 nutrients when compared to older men, and younger women had higher correlations for 7 of 13 nutrients. Median energy-adjusted Spearman rank correlation coefficients for all nutrients by gender and age-gender groups were 0.69 for younger men (range 0.55 - 0.96), 0.67 for older men (range 0.50- 0.95), 0.68 for younger women (range 0.26- 0.88), and 0.67 for older women (range 0.44- 0.87).

Table 2-4 includes Spearman rank order correlations of selected nutrient intakes estimated from the second FFQ and the average of the three 24-hour dietary recall interviews for both crude and energy-adjusted nutrient intakes. Pearson product moment correlations were also calculated, with similar results.

Intraclass correlation coefficients of the three 24-hour dietary recall interviews were calculated (Table 2-4). Intraclass correlation coefficients of the three 24-hour dietary recall interviews were similar for all age-gender groups and were somewhat lower than anticipated, indicating more variability in the three days of dietary recalls than might

Table 2-3 Ratios of mean nutrient intakes estimated from the first administration of the picture-sort food frequency questionnaire (FFQ 1) and the second administration of the picture-sort food frequency questionnaire (FFQ2). Spearman rank order correlation coefficients (r) comparing energy and nutrient intake estimates from FFQ1 and FFQ2^b. All nutrients except calories and alcohol were adjusted for total energy intake

	Males				Females			
Nutrients	\leq 69 years		> 69 years		<69 years		>69 years	
	Ratio ^a		Ratio		Ratio	r	Ratio	\underline{r}
Calories (kcals)	1.05	0.65	0.96	0.58	$0.89***$	0.72	0.95	0.70
Carbohydrates (g)	1.02	0.61	0.99	0.66	$0.87**$	0.61	0.95	0.57
Fat (g)	1.07	0.64	0.95	0.70	$0.91*$	0.72	0.96	0.67
Protein (g)	1.05	0.55	0.94	0.70	$0.92***$	0.26	$0.91*$	0.44
Fiber (g)	1.00	0.74	0.96	0.72	$0.83**$	0.63	$0.94*$	0.75
Cholesterol (mg)	1.03	0.69	0.96	0.77	$0.87*$	0.48	0.98	0.64
Water (g)	1.08	0.70	1.01	0.51	$0.95*$	0.78	0.97	0.67
Vitamin A (IU)	0.94	0.70	0.90	0.50	$0.83*$	0.66	$0.86*$	0.46
Vitamin D (IU)	0.99	0.61	$0.88***$	0.58	0.90	0.68	0.94	0.69
Vitamin C (mg)	0.95	0.68	0.93	0.67	$0.86*$	0.50	0.93	0.62
Calcium (mg)	1.04	0.69	0.95	0.66	$0.89**$	0.75	0.94	0.60
Alcohol (g)	1.34	0.96	0.75	0.95	1.03	0.82	0.24	0.87
Caffeine (mg)	1.11	0.88	1.05	0.73	0.96	0.88	0.90	0.85

^a Mean nutrient estimates from the second administration of the FFQ/ mean nutrient estimates from the first administration of the FFQ ^b Correlations above 0.26 are significantly greater than 0 at $p = 0.05$

Statistically significant different estimated mean intakes * $p < 0.05$, **p < 0.01 , ***p < 0.001 .

^a Adjusted for total energy intake using the method described by Willet et al.

^b Correlations above 0.27 are significantly greater than 0 at $p \le 0.05$.

be expected. Ranges of intraclass correlations for all age-gender groups were $0.01 - 0.47$ for macronutrients, fiber, and cholesterol; 0.30- 0.77 for caffeine, alcohol, and water; 0.02 - 0.51 for micronutrients. Intraclass correlations were lowest for fiber in older men (0.01) and highest for caffeine in older women (0.77).

Adjusting nutrient intake by the regression method reported by Willett and Stampfer 13 to obtain a measure of nutrient intake independent of total caloric intake improved correlation coefficients for most nutrients in all age-gender groups. Energyadjusted correlation coefficients ranged from 0.01 - 0.55 for macronutrients, fiber, and cholesterol; 0.22-0.83 for caffeine, alcohol, and water; and 0.15-0.70 for micronutrients. Younger men and older men had similar energy-adjusted correlations (median = 0.50 , range = $0.30 - 0.71$ for younger men; median = 0.52 , range = $0.15 - 0.62$ for older men). However, younger women had stronger energy-adjusted correlations than older women (median = 0.55 , range = $0.32 - 0.83$ in younger women; median = 0.46 , range $= 0.01 - 0.70$ for older women). Lower energy-adjusted correlations, defined here as correlations less than 0.3, were identified in older men for vitamin A and alcohol, and in older women for protein, cholesterol, vitamin A, and alcohol. No energy-adjusted correlation coefficients less than 0.30 were identified in either younger men or younger women.

Discussion

In this study three 24-hour dietary recalls and two picture-sort FFQs were used to assess the ability of the FFQ to discriminate among individuals' usual dietary intake, with reproducible results from an elderly population in Utah. It is well understood that no

known dietary assessment method gives a perfect measure of diet; however, some methods are considered more accurate than others and can be used as a comparison to test methods in validation studies 2. Here the average of three 24-hour dietary recalls collected by telephone approximately three months apart over one year's time were used to represent estimated usual intake. We chose the 24-hour dietary recall method for comparison because of its low cost, ease of administration by telephone, and relatively small respondent burden. Also, because an interviewer asks the questions and records each response, people with low literacy levels or problems with vision were not excluded. With these strengths in mind we expected that those agreeing to the validation study would be more representative of the total population than those who might agree to a more intense method of assessment would, such as weighed food records or lengthy diet histories.

We recognize several weaknesses of the telephone 24-hour dietary recall method when used as a reference method for validation studies. First, a few days of recall may not reflect a person's true usual intake. Second, the accuracy of the interview relies heavily on the short-term memory of the respondent. Third, because it is also a self-report method of dietary assessment as is the FFQ, the within-person error may be correlated to the within-person error of the FFQ. Unidentified correlated error between methods may falsely elevate correlation coefficients and lead to assumptions of better agreement between the reference method and test method than is warranted 19.

By calculating intraclass correlation coefficients using the three 24-hour dietary recall interviews we identified an unexpectedly high degree of variability in daily intake of some nutrients. The recall interviews were purposely spaced approximately 3 months apart to pick up seasonal variation in diet so some measure of variability was anticipated; however; the degree of variability was greater than expected.

Some may argue that telephone interviews may not give acceptable results in this population because of common physical limitations such as hearing loss. However, Dubois and Boivin 20 concluded after comparing telephone recalls of midday meals consumed by elderly people at congregate meal sites with data on actual intake for the meals that dietary recall collected by telephone is an acceptable way to obtain short-term dietary data from elderly subjects.

Mean intakes from the average of the three telephone 24-hour dietary recalls were similar to reported intakes of younger and older respondents 66 - 100 years old in a similar study comparing multiple 24-hour dietary recalls to picture-sort FFQs 10. Mean intakes estimated from our 137-item picture-sort FFQ were higher than those reported by Kumanyika et al. 10 , who used a similar 99-item picture-sort FFO method 15 . Adjusting nutrient intake to give a measure of intake independent of total caloric intake may aid in the comparison of correlation coefficients from our study to other studies that compare results from different dietary assessment methods. Inaccuracies in estimated absolute nutrient intake from FFQs may come from incomplete listing of possible foods, or errors in frequency and portion size estimation.

We calculated the ratio of mean nutrient intake reported from the second FFQ to the average mean nutrient intake reported from the 24-hour dietary recall interviews to evaluate the agreement of mean estimated energy and nutrient intakes between dietary assessment methods. Although ratios of mean intake were large for some nutrients in some age-gender groups, the percent of calories from carbohydrate, protein, and fat were

38

similar between methods for all age-gender groups and to those reported for elderly people in the 1987 National Health Interview Survey 15. Reports of ratios between our reference method and picture-sort FFQ were similar to results found by Larkin et al. 18 . who used a 116-item FFQ, which also included a sorting process. Nutrients with ratios furthest from one in all age-gender groups were vitamin D and caffeine. This may be due to underreporting in the 24-hour dietary recalls or overreporting in the picture-sort FFQ of single food items such as milk and coffee. Milk provided the majority of vitamin D intake in all age-gender groups (34% in men \leq 69, 45% in men $>$ 69, 54% in women \leq 69, 54% in women > 69). Similarly, coffee provides the majority of caffeine intake in all age-gender groups (73% in men \leq 69, 65% in men > 69, 84% in women \leq 69, 80% in women > 69). The ratio of alcohol intake was significantly less than one for both younger and older women (0.75, 0.33, respectively), indicating that women may underreport alcohol intake using the picture-sort FFQ.

Reproducibility of the picture-sort FFQ, as evaluated by energy-adjusted Spearman rank-order correlation coefficients and the ratio of energy-adjusted mean nutrient estimates from repeat administrations of the FFQ, for all age-gender groups, was relatively high. Spearman rank energy-adjusted correlation coefficients for all nutrients across age-gender groups ranged from 0.26 - 0.96. With the exception of protein in younger women, these correlations are generally as strong as or stronger than correlations reported by other researchers assessing reproducibility of FFQs 6, 17, 21, 22. Correlations evaluating repeatability of FFQs, reported by researchers such as Willett ⁶, Munger ²¹, Lazarus ²², Mares-Perlman ²³, and Klipstein-Grobusch ¹⁷, range from 0.41 - 0.99 for nutrients we assessed in our study.

Estimates of alcohol and caffeine intake had the strongest correlations between the first and second administrations of the picture-sort FFQ. This finding is consistent with results reported by Munger 21, Klipstein-Grobusch 17, and Mares-Perlman 23 and may be due to the low variability in the use of foods containing alcohol and caffeine.

We used Spearman rank correlation coefficients and ratios of the mean of three 24-hour dietary recalls and the second picture-sort FFQ to evaluate relative validity of the Utah Picture-sort FFQ. Energy-adjustment improved correlations for most nutrients, with the exception of alcohol. In this population where 79% of women and 82% of men reported no alcohol intake from any dietary assessment interview, alcohol and total energy intake were poorly correlated ($r = 0.140$ in men, $r = 0.098$ in women), and energyadjustment of alcohol atttenuates the correlation. Because of the lack of association between alcohol intake and total energy intake, it may be more appropriate to use unadjusted correlations when evaluating repeatability and validity of report of alcohol intake using the picture-sort FFQ.

After energy-adjustment for all nutrients with the exception of alcohol, nutrient correlations ranged from $0.01 - 0.55$ (median = 0.45) for macronutrients, fiber, and cholesterol; $0.43 - 0.83$ (median = 0.64) for alcohol, caffeine, and water; and $0.15 - 0.70$ $(median = 0.50)$ for micronutrients across all age-gender groups. In general, with the exception of protein in older women, correlation coefficients from our study were within the range of correlation coefficients reported from other studies comparing typical paperand-pencil FFQs to a reference dietary assessment method $21, 6, 17, 24$. Correlations evaluating relative validity of paper-and-pencil FFQs, reported by researchers such as Willett ⁶, Munger ²¹, Grootenhuis ²⁴, Mares-Perlman ²³, and Klipstein-Grobusch ¹⁷,

40

range from 0.14-0.83 for nutrients we assessed in our study. Correlation coefficients reported by Kumanyika et al. 10 , who also compared a picture-sort FFQ to multiple dietary recalls in an elderly population, found correlations with ranges from 0.22 - 0.61 for macronutrients, fiber, and cholesterol; and 0.18 - 0.58 for micronutrients. Alcohol, caffeine, and water were not studied. As compared to Kumanyika's study, we report somewhat lower correlations for macronutrients and higher correlations for micronutrients.

Although correlations from our study did include ranges with lower limits, these lower correlations were seen only in older men and women > 69 years. This may suggest that respondents' ability to accurately report usual intake with our picture-sort FFQ and possibly with other dietary assessment methods, including 24-hour dietary recalls, may progressively decrease with age.

Calculating correlation coefficients and other statistics by age-gender strata enabled us to assess differences by gender as well as differences between respondents \leq 69 years and those $>$ 69 years within gender. Differences between age-gender groups were noted for statistics used to compare mean nutrient estimates and to assess reproducibility and validity. In general, it appears that younger respondents (≤ 69) years) may report usual nutrient intake by using the picture-sort FFQ slightly more accurately than do older respondents(> 69 years). Because of known physical and cognitive limitations that naturally occur with increasing age, this is not surprising. Limitations imposed on respondents as they age may hinder their ability to accurately report nutrient intakes using any dietary assessment method. Although we report lower correlations between methods and administrations for respondents > 69 years as

compared to respondents ≤ 69 years, we believe these same differences may be identified in other elderly populations by using other dietary assessment methods. This difference in ability to accurately report nutrient intake may not be a function of the picture-sort FFQ method but rather a function of problems and limitations associated with increasing age. Further study should be conducted on repeatability and validity of dietary assessment methods for elderly populations extending the upper age groups to include those in their eighties and nineties and then comparing performance between subgroups of elderly men and women based on age.

Conclusion

Our data suggest that structuring the FFQ as a two-step process of sorting food picture cards into period of use and then reporting frequency of use per period gives a useful measure of usual dietary intake. Correlation coefficients comparing the Utah picture-sort FFQ to a measure of usual dietary intake were comparable to correlation coefficients reported in other validation studies comparing traditional FFQs as well as other picture-sort FFQs to reference methods. Although we did not conduct formal process evaluations, we believe picture cards may allow better identification of foods in respondents with poor reading skills or impaired vision, and that the sorting process itself may improve cognitive orientation to the task of assigning accurate frequency of use to specific foods. Research on using cognitive interviewing to improve FFQs suggests that the manipulation of cards may positively influence the response process by providing visual, tactile, and motor involvement 25 . In the future, it would be helpful to conduct formal tests of process and sensory evaluation between a picture-sort FFQ and a

traditional paper-and-pencil FFQ. Results from such process and sensory evaluations may make it clearer whether the picture-sort FFQ offers a significant advantage over traditional FFQs in populations where poor vision or limited literacy and language skills are common.

References

- I. Thompson FE, Byers T. Dietary assessment resource manual. J. Nutr. 1994; **124:** 2245S - 2317S.
- 2. Willett WC. Nutritional Epidemiology. New York: Oxford Press, 1990.
- 3. Van Staveren WA, de Groot LC, Blauw YH, van der Wielen RP. Assessing diets of elderly people: problems and approaches. Am. J. Clin. Nutr. 1994; 59: 221 S-223S.
- 4. Kumanyika SK, Tell GS, Shemanski L, Martel J, Chinchilli VM. Dietary assessment using a picture-sort approach. Am. J. Clin. Nutr. 1997; 65: 1123S-1129S.
- 5. Freedman LS, Carroll RJ, Wax Y. Estimating the relation between dietary intake obtained from a food frequency questionnaire and true average intake. Am. J. Epidemiol. 1991; 134: 310-20.
- 6. Willett WC, Sampson L, Stampfer MJ. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am. J. Epidemiol. 1985; **122:** 51- 65.
- 7. Willett WC, Reynolds RD, Cottrell-Hoehner S, Sampson L, Browne ML. Validation of a semi-quantitative food frequency questionnaire: comparison with a 1-year diet record. J. Am. Diet. Assoc. 1987; 87: 43-7.
- 8. Willett WC, Sampson L, Browne ML, Stampfer MJ, Rosner B, Hennekens CH, Speizer FE. The use of a self-administered questionnaire to assess diet four years in the past. Am. J. Epidemiol. 1988; **127:** 188-99.
- 9. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. A databased approach to diet questionnaire design and testing. Am. J. Epidemiol. 1986; **124:** 453-69.
- 1 0. Kumanyika S, Tell GS, Fried L, Martel JK, Chinchilli VM. Picture-sort method for administering a food frequency questionnaire to older adults. J. Am. Diet. Assoc. 1996; 96: 137-44.
- 11. Posner BM, Smigelski C, Duggal A, Morgan JL, Cobb J, Cupples LA. Validation of two-dimensional models for estimation of portion size in nutrition research. J. Am. Diet. Assoc. 1992; 92: 738-41.
- 12. Johnson RK, Driscoll P, Goran MI. Comparison of multiple-pass 24-hour recall estimates of energy intake with total energy expenditure determined by the doubly labeled water method in young children. J. Am. Diet. Assoc. 1996; 96: 1140-4.
- 13. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol. 1986; **124:** 17-27.
- 14. Beaton GH, Milner J, Corey P, et al. Sources of variance in 24-hour dietary recall data: implications for nutrition study design and interpretation. Am. J. Clin. Nutr. 1979; 32: 2546-9.
- 15. Block G SE. Estimate of nutrient intake from a food frequency questionnaire: The 1987 National Health Interview Survey. J. Am. Diet. Assoc. 1992; 92: 969-977.
- 16. Mares-Perlman JA, Klein BE, Klein R, Ritter LL, Freudenheim JL, Luby MH. Nutrient supplements contribute to the dietary intake of middle- and older-aged adult residents of Beaver Dam, Wisconsin. J. Nutr. 1993; **123:** 176-88.
- 17. Klipstein-Grobusch K, Den Breeijen JH, Goldbohm RA, et al. Dietary assessment in the elderly: validation of a semiquantitative food frequency questionnaire. Eur. J. Clin. Nutr. 1998; 52: 588-96.
- 18. Larkin FA, Metzner HL, Thompson FE, Flegal KM, Guire KE. Comparison of estimated nutrient intakes by food frequency and dietary records in adults. J. Am. Diet. Assoc. 1989; 89: 215-23.
- 19. Kipnis V, Carroll RJ, Freedman LS, Li L. Implications of a new dietary measurement error model for estimation of relative risk: application to four calibration studies. Am. J. Epidemiol. 1999; **150:** 642-51.
- 20. Dubois S, Boivin JF. Accuracy of telephone dietary recalls in elderly subjects. J. Am. Diet. Assoc. 1990; 90: 1680-7.
- 21. Munger RG, Folsom AR, Kushi LH, Kaye SA, Sellers TA. Dietary assessment of older Iowa women with a food frequency questionnaire: nutrient intake, reproducibility, and comparison with 24- hour dietary recall interviews. Am. J. Epidemiol. 1992; 136: 192-200.
- 22. Lazarus R, Wilson A, Gliksman M, Aiken J. Repeatability of nutrient intakes estimated by a semiquantitative food frequency questionnaire in elderly subjects. Ann. Epidemiol. 1995; 5: 65-8.
- 23. Mares-Perlman JA, Klein BE, Klein R, Ritter LL, Fisher MR, Freudenheim JL. A diet history questionnaire ranks nutrient intakes in middle-aged and older men and women similarly to multiple food records. J. Nutr. 1993; **123:** 489-501.
- 24. Grootenhuis PA, Westenbrink S, Sie CM, de Neeling JN, Kok FJ, Bouter LM. A semiquantitative food frequency questionnaire for use in epidemiologic research among the elderly: validation by comparison with dietary history. J. Clin. Epidemiol. 1995; **48:** 859-68.
- 25. Lieberman LS, BobroffLB, Probart CK, Kurtz CS. A visual tool for improved cross-cultural dietary assessment. Am. J. Clin. Nutr. 1994; **59S:** 290S (abstract).

CHAPTER 3

DIETARY PROTEIN INTAKE AND RISK OF HIP FRACTURE IN THE ELDERLY: A REVIEW

Abstract

Osteoporosis, characterized by low bone mass and structural deterioration of bone tissue, is a major public health threat. Hip fractures are the most serious of all fractures related to osteoporosis and cause disability and excess mortality in the elderly. Although protein has received less attention in research pertaining to osteoporosis than other nutrients, it appears to play an important role in bone health and thus risk of hip fracture. Protein intake increases urinary calcium excretion, yet in the presence of adequate dietary calcium intake may not disrupt calcium balance. Protein is an important component of the bone matrix, and protein supplementation improves medical outcomes and levels of insulin-like growth factor-1 (IGF-1) after hip fracture in the elderly. IGF-1 , known to be osteotrophic, decreases with age and with protein-depletion. However, results from observational studies are controversial and while some report negative associations between protein intake and risk of hip fracture others do not. Future directions in research pertaining to protein's role in bone health, including examination of source of protein intake by food groups, and specific amino acids implicated in bone metabolism, may help to clarify the relationship. Although confounders in the relationship make the association less clear, current evidence suggests that higher dietary protein intake from varied food sources may be more beneficial than harmful in the elderly who are at increased risk for bone loss and associated hip fractures.

Introduction

Osteoporosis, a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fracture, is a major global public health threat. Seventy percent of all fractures in persons aged 45 years or over are due to osteoporosis (1). Although osteoporotic fractures have plagued the elderly of industrialized countries in North America and Europe for decades, they also pose an emerging problem in developing countries of Africa and Asia (1). The aging of populations worldwide will inevitably raise the already enormous financial and health-related costs associated with osteoporotic fractures.

Hip fractures are the most serious of all osteoporotic fractures (2). It is estimated that 90% of hip fractures occur in men and women with reduced bone strength who fall from a standing height or less (I) (2). Osteoporotic hip fracture is often thought of as a condition of aging women, but hip fracture rates increase exponentially with age for both men and women. Because there are more elderly women than men, about 80% of all hip fractures occur in women although age-specific incidence rates of men lag those of women by only five to seven years (1) (2). The estimated lifetime risk of suffering a hip fracture is 6.0% in white men and 17.5% in white women (3).

Adverse outcomes of osteoporotic hip fractures are associated with morbidity, mortality, and economic cost. One year after hip fracture, 40% of patients cannot walk alone, 60% have difficulty with at least one essential activity of daily living, 27% have been admitted to a nursing home for the first time, and 20% have died (4). Ultimately up to one third of all people who suffer from a hip fracture become totally dependent and many require lifetime institutionalization (1). Nursing home care is extremely costly and

accounts for approximately half of the direct cost of hip fracture in the United States, estimated at 10 - 20 billion dollars annually (1) (5). The constant aging of the population is expected to drive the annual direct cost of hip fracture in the United States to near 240 billion dollars within the next 50 years (5).

Osteoporosis has been described as a continuum, not a sudden event, and many modifiable and unmodifiable risk factors play a role in its etiology through the life-cycle. Risk factors for osteoporosis can also be implicated as risk factors for hip fracture and most involve pathways associated with increased skeletal fragility and decreased bone mineral density (BMD) or increased risk of fall-related trauma (2). Identified unmodifiable risk factors for osteoporosis include: white race, female gender, family history and small body frame (6). Modifiable risk factors include: cigarette smoking, excessive caffeine and alcohol intake, and low physical activity (6).

Several nutrition-related factors are also among modifiable risk factors for osteoporosis and related hip fracture. Dietary interventions for the prevention and treatment of osteoporosis have long been focused on a few select nutrients including calcium, phosphorous, and vitamin D. Other nutrients, including protein, have been less well studied but may also play an important role in bone health and thus risk of fracture.

A growing body of evidence supports the hypothesis that dietary protein plays an important role in bone health, although the role of dietary protein in risk of hip fracture remains controversial. Protein is an important component of the bone matrix upon which bone mineralization occurs (7). Protein-energy malnutrition (PEM) is common among elderly hip fracture patients, and medical outcomes after hip fracture improve with protein supplementation. Dietary recommendations for protein intake in the elderly are

debatable, and current recommendations may not meet needs. Some (8-11), but not all (12), observational studies found a positive association between protein intake and bone mineral density, yet several (13-15), but not all (16), report higher fracture rates in groups with high intakes of protein. Protein intake may be related to calcium balance and increased protein intake may increase urinary calcium loss. In this paper, literature surrounding these avenues by which protein may be related to risk of hip fracture in the elderly will be reviewed, and areas of further research that may help to clarify this complex and perplexing relationship will be proposed.

Protein and Calcium Balance

Human Studies

In early research pertaining to bone health protein was viewed largely in terms of how it influences calcium balance. It has long been known that dietary protein intake and calcium balance are interrelated. As early as 1942 researchers found a positive correlation between protein intake and retained calcium (17). Dietary restrictions in Great Britain during World War II led researchers to study the effect of dietary rationing on calcium deficiency. They found volunteers who consumed low levels of protein (45- 70 grams) had lower calcium absorption (2.8 - 8.1%) than when the same volunteers consumed higher levels of protein (100 - 130 grams). In this somewhat crude study, higher levels of dietary protein boosted calcium absorption to as much as 16. 9%. Although early researchers also observed an increased urinary excretion of calcium at high levels of protein, this phenomenon was not explored until later.

In 1968 Wachman and Bernstein put forth the hypothesis that diets high in meat and animal protein elevate metabolic acid production and lead to chronic bone buffering and loss (18). In the 1970's and 1980's serious attention was given to this possibility, and several animal and human studies were published examining the effects of excessive dietary protein intake on bone (Table 3-1). Many early metabolic studies were short-term (15-days), emolled young adult males, and altered the diet by increasing protein intake to higher than normal levels by addition of purified protein supplements (19-21). Although results are often compared between studies, many factors such as the amount and source of protein, calcium, and phosphorous provided are highly variable between studies. All published studies from Johnson et al. , Walter et al., and Anand et al. , report increased urinary calcium excretion with high (141-142 g/day) purified-protein diets. In a study maintaining calcium intake at 1400 mg and increasing protein intake to 141 g/day, calcium absorption appeared to be increased (19); however, in similar studies maintaining calcium intake at 800 mg/day (20) and 500 mg/day (21) an increase in calcium absorption was not observed. Heaney and Recker (22) aggregated data from 11 experiments, all of which increased protein intake from isolate protein sources, examined the relationship of relative urinary calcium excretion to relative protein intake and found a doubling of protein intake produced about a 50% increase in urinary calcium excretion.

Amount of calcium intake may play a critical role in overall calcium balance during periods of high protein intake. A negative calcium balance was observed in subjects consuming diets including 500 mg of calcium and 95 g of protein (20) but not in subjects consuming diets including 800 mg of calcium and 95 g of protein (21). The degree to which urinary calcium excretion adversely affects bone may in part depend on

Table 3-1 Results from human metabolic studies on dietary protein and urinary calcium excretion

52

level of calcium intake, and Heaney proposed that a ratio of 1 g protein to 20 mg calcium may protect against the bone loss associated with high protein diets (23)

Early metabolic studies conducted on young adult males over short periods of time say little about protein's long-term effect on bone health or its effect in female and aging populations. In a longer term (1 05 day) metabolic study, young men and women fed high isolate protein diets (36g/day Nitrogen) including 1400 mg calcium had increased urinary calcium excretion that did not decline after time (24). Contrary to previous reports (17, 19), there were no differences in the absorption of calcium for subjects consuming long-term adequate or high protein diets. Osteoporotic patients receiving high purified protein diets (2 g/kg/day) had increased urinary calcium and negative calcium balance without change in calcium absorption (25). A significant positive correlation between daily urinary excretion of calcium and protein intake, especially animal protein intake, was observed in a cross-sectional study of healthy elderly adults in Japan (aged 50- 79 years) (26).

As illustrated above human metabolic studies generally indicate addition of purified proteins to a diet increases urinary calcium excretion and may result in bone loss. However, the effect of increasing protein intake from real food sources may have a different effect on calcium metabolism. Other nutrients commonly found in foods high in protein and not in isolate protein supplements, such as phosphorous and calcium, may blunt the effect of protein on urinary calcium excretion.

Longer term studies of Spencer et al. (27) examined the effect high protein intake from meat (2 g/day) had on calcium metabolism in the presence of different dietary calcium intakes in older adult males (40 - 67 years old). As was speculated, the increase

in urinary calcium as previously observed with addition of protein isolates was blunted, and high protein intake obtained from meat in the presence of low (200 mg/day), normal (800 mg/day), or high $(>=1100 \text{ mg/day})$ calcium intake did not significantly increase long-term urinary calcium excretion. Additionally, results from these and one other similar study (28) found neither calcium absorption nor balance were affected by protein intake when the protein was obtained from meat or other food sources.

Pannemans et al. (29) studied the effect of increasing dietary protein from 12%- 20% of total energy on urinary calcium excretion in elderly males. Urinary calcium excretion was not different during the normal and high protein diets, and calcium balance during the high protein diet was improved over calcium balance during the normal protein diet. High-protein intake of 2 g/kg/day obtained in an equal ratio of animal to vegetable protein did not increase urinary calcium excretion in elderly male volunteers 66 - 88 years of age (30). In a metabolic study of older women 41 - 70 years of age, high meat consumption did not compromise calcium balance or increase urinary calcium excretion (31). These and other studies finding no increase in urinary calcium excretion from high protein diets of food sources stimulated additional interest in defining the mechanism of action for protein induced calciuria and the importance of phosphorus and calcium as modulating elements in calcium balance.

Animal Studies

In addition to the human studies discussed above, several animal studies of rats and mice have been conducted to examine the effect of high protein intake on calcium balance and bone metabolism (32-35). Most studies conclude that unlike humans, bone homeostasis in adult rodents is not sensitive to excess protein. Although high protein

intakes induced increases in urinary calcium excretion, fractional loss of endogenous calcium was reduced and bone homeostasis was conserved (32) (35). Therefore, rodents may not be the model of choice for studying protein-induced bone loss in humans.

Acid-Ash Osteoporosis Hypothesis

Wachman and Bernstein proposed that a long-term high protein intake may lead to metabolic acidosis resulting in increased bone resorption, release of calcium from bones, increased urinary calcium excretion, and eventually in the development of osteoporosis (18). Endogenous acid produced by the metabolism of high protein foods correlates with urinary calcium excretion (36).

The average American diet, high in protein and low in fruits and vegetables, generates over 100 mEq of acid daily in the forms of phosphate and sulfate (37). Whiting and Draper (32) found a linear relationship between urinary calcium and sulfate excretion in rats and hypothesized that the variability in the calciuretic response to different protein intakes was mainly related to differences in the content of sulfur containing amino acids. However, in a human study the addition of sulfur containing amino acids to a low protein diet in the amount contributed by a high protein diet accounted for only 43% of the increase in urinary calcium observed with the high protein diet (38).

Neutralization of endogenous acid may improve calcium balance and reduce bone resorption. In a study of postmenopausal women, potassium bicarbonate neutralized endogenous acid and improved calcium balance reducing bone resorption (36). Diets high in foods with a positive potential renal acid load (fish, meat, grain products, and cheese) cause bone loss by inducing mobilization of calcium from bone, but foods with a negative potential renal acid load (milk, non-cheese dairy products, fruits, vegetables)

55

produce alkali-ash, neutralize acid-ash and prevent calcium mobilization from bone (37). From the study of Dietary Approaches to Stop Hypertension (DASH) we learn that increasing fruit and vegetable intake from 3.6- 9.5 daily servings significantly decreased urinary calcium excretion when protein was held at a constant percent of energy (39). This decrease in urinary calcium excretion may be a direct result of increased production of alkali-ash from the addition of fruits and vegetables.

Mechanisms of Protein Induced Hypercalciuria

There is little doubt that increasing dietary protein in the form of purified protein stimulates increased urinary calcium excretion. Possible mechanisms for this response include enhanced intestinal absorption of calcium, increased glomerular filtration rates, and inhibition of renal tubular reabsorption (27) (40-42).

Although increasing protein from low to adequate intake has been documented to increase calcium absorption (17), there is little evidence to conclude that increasing protein intake from adequate to high intake has the same effect. Heaney (43) recently reported an absence of relation between calcium absorption efficiency and protein intake in adult women consuming 0.4- 1.96 grams protein/kg/day and concluded that because protein increased urinary calcium loss without an increase in absorption, overall calcium loss may result. Whether this effect results in negative calcium balance depends on the amount of calcium in the diet (20-21). In a longitudinal study of bone health in young adult women, rate of gain in bone density was positively correlated with ratio of dietary calcium to protein (44). Furthermore, increased protein in self-selected diets is usually accompanied by increased calcium (45). Some believe a dietary calcium-to-protein ratio

 of > 20 mg calcium to one g protein may provide adequate protection against calcium loss from the skeleton (23) (43).

Dietary protein affects the renal handling of calcium and is associated with increased urinary calcium excretion. High protein diets increase glomerular filtration rate and decrease tubular calcium reabsorption in the nephron (24) (40) (46). Phosphorous, on the other hand, increases tubular reabsorption and consequently decreases urinary calcium excretion (47). Decreased tubular calcium reabsorption accompanying high protein intake may be due to the effects of an increased acid-ash load on the renal tubular cells (42). Kim and Linkswiler (46) reported that in the presence of a high protein diet, glomerular filtration rate increased by 10% and renal tubular reabsorption of calcium decreased by 1%.

Summary

Variation in the design of studies examining the effect of dietary protein intake on calcium metabolism and bone health makes it difficult to compare results between studies. Variables of interest that may affect protein's relationship to calcium and bone metabolism include source of protein, duration of the study, characteristics of the study population, levels of calcium, phosphorous, sodium, and fruit and vegetable intakes, as well as a host of other confounders. Conclusions must be drawn with caution. Protein does appear to increase urinary calcium excretion although other nutrients found in foods containing protein may modify protein's affect on calcium and bone metabolism. Furthermore, interactions between protein intake and other nutrients such as calcium and phosphorous, or other risk factors such as age, physical activity, and estrogen use may

cloud the association between protein intake and calcium balance, bone health, osteoporosis, and risk of hip fracture.

Protein Deficiency in the Elderly

Malnutrition or under-nutrition is often observed in the elderly (48-50) and may be more prevalent in people with hip fracture than in the general aging population (11) $(51-52)$. Wilson et al. (49) identified undernutrition in 11% of elderly persons attending hospital outpatient clinics; Jensen et al. (53) observed malnutrition in 59% of elderly patients admitted to a hospital for hip fracture. Other studies have reported similar findings (54-57). Age related factors which may inhibit the elderly's ability to meet nutritional requirements include a decline in physical activity leading to reduced food intake, a decline in nutrient absorption efficiency and renal conservation of nutrients, as well as changes in socioeconomic status, taste, appetite, and the ability to cut and chew foods such as meat and raw fruits and vegetables (48).

Protein is the most common nutrient deficiency in persons 65 years of age or older (51), and protein-energy malnutrition (PEM) is the deficiency observed most often in patients with hip fracture (53) (58-59). Levels of serum albumin along with serum prealbumin, transferrin, insulin-like growth factor 1 (IGF-1), and total lymphocyte count are often used as markers for protein status (54-55). Hip fracture patients with low serum albumin levels had higher rates of mortality (59) and longer than average hospital stays (60) than did patients with normal serum albumin levels. In one observational study, very thin, undernourished elderly hip fracture patients with low serum albumin levels had four times the mortality rate as the same aged well-nourished hip fracture patients (61).

Protein depletion in hip fracture patients is correlated with complications such as poor healing, infection, delayed physical rehabilitation, and increased mortality (53) (55).

Protein Deficiency and Fracture Risk

Although deficiencies of other nutrients such as calcium, phosphorous, and vitamin D are often implicated in the pathology of bone loss, deficiency of protein may be particularly important in relation to the risk of hip fracture (58) (62). Hospitalized elderly patients whose protein intakes were greater than $1 \frac{g}{kg}$ day had higher BMD than the same aged patients whose protein intakes were less than $1 \frac{g}{kg}$ day (11).

Protein is crucial to the structure of bone matrix, and dietary protein deficiency could negatively affect the balance between bone formation and bone resorption (51). In aged rats, a reduction in dietary protein intake decreased bone density, mass, and strength in both cancellous and cortical bone (63). Protein deficiency may also contribute to the occurrence of hip fracture by impairing movement coordination, diminishing the protective layer of soft tissue padding, and reducing muscle strength, all of which may increase propensity to suffer a fracture due to a fall (58) (64-65).

Protein Requirements in the Elderly

Although many agree that elderly people are at increased risk for protein-energymalnutrition (PEM), with the prevalence well documented in hospitalized patients, much debate exists regarding recommendations for protein requirements in the elderly. Current research may indicate protein needs in later years are greater than current standard recommendations (Table 3-2). The current Recommended Dietary Allowance (RDA) for

protein, 0.8 g protein/kg/day, was set as the safe and adequate intake for virtually all healthy men and women aged 19 years and older (66). The 1985 FAO/WHO/UNU consultation also suggested that protein needs are similar in elderly and young adults and estimated the mean protein requirement for all adults to be 0.6 grams/kg/day (67). After traditional upward adjustment of the mean requirement, 0.75 grams protein/kg/day was set as the safe level of intake estimated to meet metabolic needs of 97.5% of adults across the world aged 19 years or older (67).

Table 3-2

Current recommendations and conclusions from protein requirement studies in elderly people

Recommendations for protein requirements in the elderly were made in light of several limitations pertaining to the research studying nitrogen balance in older people. At the time current recommendations were set, few studies had been conducted on elderly people, and results from existing studies were conflicting with estimated mean protein requirements ranging from 0.46-0.83 grams/kg/day (68-71). Recommendations for aging men and women were at large extrapolated from nitrogen balance studies of young

men taking into account age-associated changes in body composition of the elderly, including loss of lean muscle mass (67). Thus, with regard to lean body mass, recommended dietary protein intake in grams/kg body weight was greater for elderly than young adults.

This possible increase in protein requirement per kg body weight in elderly adults over younger adults may be at least partly attributed to the less efficient protein utilization observed in elderly subjects (72). Other factors that may affect protein requirements in the elderly include the presence of chronic disease, changes in physical capacity and activity, a decline in total energy intake, changes in metabolic status and function, as well as medication use (73-74). However, based on the limited research available, current standards seem to be somewhat crude.

Limitations in the methodology of early nitrogen balance studies may have contributed to the conflicting results and wide range of reported recommended mean intakes. Early studies commonly overestimated nitrogen balance by failing to recognize miscellaneous nitrogen loss, and thus underestimated nitrogen requirements. The FAO/WHO/UNO consultation recommended a standard formula for assessing nitrogen balance. This formula included a standard 8 mg nitrogen/kg/day miscellaneous nitrogen loss factor (72), underreported or unaccounted for in earlier studies. Campbell et al. (73) reassessed the nitrogen balance data from several early studies published by Zanni et al. (68), Cheng et al. (69), and Uauy et al. (71), and a weighted average mean protein requirement of 0.89 grams protein/kg/day was estimated.

Additional evidence from more recent nitrogen balance studies of elderly people also indicates the safe level of protein intake for older adults may be higher than current

61

recommendations. Bunker et al. (75) studied healthy and homebound elderly men and women aged 70 - 86 years consuming self-selected diets. Healthy elderly participants maintained nitrogen equilibrium at daily protein intakes of 0.97 g protein/kg/day. Homebound elderly were in negative nitrogen balance at mean protein intake of 0.67 g/kg/day. However, these calculations did not allow for miscellaneous nitrogen losses and thus may have overestimated nitrogen balance. While limitations of the study prevented the authors from inferring a recommended intake, they concluded a protein intake of greater than 0.8 g/kg/day was needed to maintain nitrogen equilibrium in elderly people.

Campbell et al. (73) studied two groups of elderly men and women consuming weight-maintenance diets providing either 0.8 or 1.6 g protein/kg/day. Subjects consuming 0.8 g protein/kg/day were observed to be in negative nitrogen balance whereas subjects consuming 1.6 g protein/kg/day were observed to be in positive nitrogen balance. After regressing nitrogen balance data on mean protein, it was estimated that a mean intake of 1.0 g protein/kg/day is required for nitrogen equilibrium in the elderly.

Alternative methods and outcomes to nitrogen balance studies have also been used to assess protein requirements in the elderly. Castaneda et al. (76) assessed outcomes such as changes in lean tissue mass, immune response, and muscle function as markers for protein requirements. In a 9-week study elderly women were assigned weight maintenance diets containing either 0.45 or 0.92 g protein/kg/day. Participants in the low protein intake group showed significant losses in anthropometric measures and immune
function although weight remained stable. Participants in the high protein group showed no similar changes in anthropometric measures or immune function.

Data from recent nitrogen balance studies as well as retrospective reassessment of earlier balance studies seem to imply that dietary requirements of the elderly exceed current recommendations of 0.8 g protein/kg/day and may be more in the range of 1.0 g protein/kg/day (73) (77). In one sample of almost 700 free-living healthy elderly men and women average protein intake was $1.01 - 1.06$ g/kg/day (78). A 10-year longitudinal study of 304 initially healthy elderly women showed women with protein intakes greater than 1.2 - 1.7 g/kg/day developed fewer health problems than those with protein intakes \leq 0.8 g/kg/day (79). Additional research including alternative methods of assessing nitrogen balance as well as standardization in study methodologies are needed before a mean protein requirement may be established with confidence for the elderly.

Protein Supplementation in Hip Fracture

Protein-energy-malnutrition may contribute to the occurrence of hip fracture and is commonly observed in elderly people hospitalized for hip fracture. Protein deficiency may adversely influence clinical outcome after hip fracture, and several intervention studies have shown that patients given daily oral supplements containing protein have fewer post fracture complications (52) (65) (74) (80-81). The mechanism of how protein influences recovery time, functionality, medical complication, and mortality after hip fracture is still a matter of debate.

Delmi et al. (80) studied the effect of oral supplementation on clinical outcome of elderly patients with hip fracture. Nutritional requirements of study participants were not

met during hospital stays for hip fracture, and voluntary intake of protein was only 60% of the daily recommended intake. Patients receiving a daily oral nutrition supplement containing 20 g of protein, 254 kcals, and selected vitamins and minerals had shorter median hospital stays (24 vs. 40 days) and lower rates of complications and mortality than patients not receiving the daily supplement. However, because the oral supplement contained many nutrients, protein could not be identified as the nutrient responsible for the favorable outcomes. In fact, Delmi et al. hypothesized that the beneficial effects may have been due to the vitamin A content in the supplement, not protein.

Protein was targeted as the possible nutrient improving clinical outcome in another similar investigation in which elderly hip fracture patients were randomized to either receive a protein-containing supplement or a similar non-protein-containing supplement (52). Normalization of protein intake during hospitalization attenuated loss ofBMD in the femoral shaft observed at 7 months post fracture. A more pronounced increase in osteocalcin, a marker of osteoblast activity, was observed in the protein supplement group than in the non-protein supplement group (58). Furthermore, patients receiving the protein supplementation had fewer complications than patients not receiving the protein supplementation.

The effect of protein intake on insulin-like growth factor (IGF) was studied in a randomized, placebo-controlled trial of oral supplementation of hip fracture patients (65). IGF, known to decrease with age and with dietary protein restriction, may enhance bone formation through direct action on osteoblasts, bone-forming cells (52) (82). Consistant with findings from other studies (52) (74) (80-81), results indicated protein supplementation after hip fracture was associated with shorter hospital stays, fewer

complications, and attenuation of bone mineral loss in the months following fracture, as well as increased IGF-1 levels.

Although many studies report improvement in clinical outcomes post hip fracture during oral protein supplementation, few have examined the relationship between protein supplementation and functional recovery. One year after hip fracture, 40% of patients cannot walk alone (4), and mobility can be used as a marker of functional recovery. In a recent randomized trial where elderly hip fracture patients received a protein containing oral supplement or placebo, no difference was observed in functional ability or mobility at six months post fracture (81). More than 50% of participants in both the treatment and control groups returned to pre-fracture levels of mobility at 6 months.

While there seems to be little question that normalization of protein intake post hip fracture reduces recovery time, hospital stay duration, rates of complication, and attenuates bone mineral loss, small randomized, placebo-controlled trials cannot answer the larger question of whether adequate protein intake can prevent osteoporosis and reduce risk of hip fracture in the elderly.

Protein and Insulin-Like Growth Factor

Dietary protein may influence bone health and hip fracture risk through several possible mechanisms, some of which were described in previous sections. Protein is an important component of the bone matrix, and deficiency may disrupt the balance between bone formation and bone resorption. Protein deficiency may decrease muscle strength and impair movement coordination and balance, thus increasing the propensity to fall and

decreasing the force needed to fracture a hip because of a fall. Protein may also influence bone health through its effect on insulin-like growth factor (IGF-1).

Both aging and protein-energy restriction are associated with a decrease in growth hormone (GH) secretions and lowered levels of IGF-1 (82-83). IGF-1 promotes bone formation by direct stimulation and activation of osteoblasts (84). Insulin-like growth factor 1 is synthesized in the liver and bone and is regulated by hormones including estrogen, parathyroid hormone (PTH), and 1 ,25-hydroxyvitamin D3 (83). Elderly hip fracture patients consuming low levels of protein had low levels of IGF-1, which returned to normal after protein supplementation (65) . In a study of healthy men, IGF-1 and its major binding protein (BP) IGFBP-3 were both positively correlated to muscle strength, and total body BMD (83). Castaneda et al. (85) found elderly women fed marginal protein diets $(0.45 \text{ g protein/kg/day})$ for 10 weeks had low levels of IGF-1 which were associated with loss of skeletal muscle mass. Furthermore, plasma IGF-1 concentrations seem to be a reliable biochemical index for identifying protein-energy-malnutrition in the elderly (85-86).

Mechanisms of Action

Recent findings from animal studies further elucidate the cellular mechanism involved in the relationship between dietary protein intake, serum levels of IGF-1, and bone health. In a study of aged male rats, a reduction in dietary protein intake decreased IGF-1, BMD, bone mass, and bone strength in both trabecullar and cortical bone (63). Bourrin et al. (63) observed similar numbers of osteoclasts, responsible for bone resorption, in rats fed low and high protein diets; however, parameters of bone formation were depressed in only the low protein diet group. A similar study in female rats

demonstrated that protein-restriction also causes I GF **-1** resistance in remaining osteoblasts (87). Injections of IGF-1 to protein-restricted rats did not result in increased bone formation or osteocalcin levels (87). Furthermore, the effects of low IGF-1 induced by a low protein diet and altered sex hormone levels, as seen after menopause in women, and studied in ovariectomized adult female rats, may be additive (88).

Several investigators agree that the mechanism of bone loss in response to low protein intake seems to be a decrease in bone formation due not only to the reduction in osteoblast recruitment but also to osteoblast resistance to stimulation and activation by IGF-1 and thus reduction in the amount of bone matrix deposited per unit of bone (87) (88). Indeed, null findings from a study of IGF-1 treatment and impact on bone mineral density (89) may be explained by osteoblast resistance to IGF-1 in response to inadequate protein intake.

Observational Studies: Protein Intake and Bone

Cross-Cultural Surveys

Marked variation in hip fracture incidence between populations of different geographic regions as well as within populations of specific geographic regions suggests an important role for environmental factors, such as nutrition, in risk of hip fracture (2). Nutrients such as calcium and vitamin D are often implicated as risk factors for osteoporosis and hip fracture, but other nutrients, such as protein, have received far less attention.

Abelow et al. (15) examined cross-cultural variations in animal protein consumption and hip fracture incidence from 16 countries. As expected, animal protein

consumption was greater in industrialized countries such as the United States and Great Britain than those of developing countries in Asia and Africa. Regression of age-adjusted fracture rates against estimated dietary animal protein intake indicated a strong positive association. In this multi-country survey, calcium and protein intake were highly correlated $(R = 0.91, p = 0.001)$, and it was proposed that calcium intake may be a crosscultural marker for animal protein-rich diets. Findings from this cross-cultural study are consistant with the hypothesis that diets high in meat and animal protein elevate metabolic acid production and lead to chronic bone buffering and loss (18).

In a second cross-cultural study, Frassetto et al. (90) examined worldwide incidence of hip fracture in elderly women by ratio of vegetable to animal food consumption. Countries with low ratios of vegetable to animal food had high incidence of hip fracture. Furthermore, after adjustment for total protein intake, vegetable food consumption was a negative predictor of hip fracture incidence. Frassetto and colleagues hypothesized the observed protective effect was associated with base precursors from vegetable foods balancing acid precursors from animal foods and preventing chronic bone buffering, as proposed in the acid-ash osteoporosis theory.

Population-Based Studies

Although cross-cultural studies conclude animal protein may be associated with increased incidence of hip fracture, many population-specific observational studies give evidence supporting a protective role of protein in bone health.

Findings from observational studies examining the relationship between dietary protein intake and bone health are summarized in Table 3-3. Five of eight studies cited

Table 3-3

Reports from observational studies examining the relationship between dietary protein intake and bone health

provide evidence that protein plays a protective role in risk of osteoporotic hip fracture while four of nine provide evidence to the contrary. Results, taken collectively, should be interpreted cautiously. Inherent differences in study designs such as quantification of protein intake, measurements of bone health or risk to fracture, and population characteristics such as age, gender, and race make it difficult to compare conclusions between studies and thus results appear controversial.

Few reports from prospective studies examining the relationship between protein intake and bone health with actual incident hip fracture as the outcome measure have been published. In The Nurses' Health Study, dietary protein intake was positively associated with an increased risk of forearm fracture however, no association was observed with risk ofhip fracture (14). In a Norwegian study, adult men and women answered a semi-quantitative dietary questionnaire and were followed for 11 years with respect to hip fracture (13). An elevated risk of hip fracture was found in participants with a high intake of non-dairy protein in the presence of low calcium intake. However, no similar effect was observed for total protein or non-dairy animal protein independent of calcium intake. In the Iowa Women's Health Study, postmenopausal women with higher intakes of total protein and animal protein had a lower risk of hip fracture than women with lower intakes (16).

Several studies have examined the relationship between dietary protein intake and bone health using BMD or change in BMD over time as a marker for bone health. Most (8) (10-11) (91) but not all (12) found a positive association between protein intake and BMD. In a cross-sectional study of pre- and postmenopausal women, dietary protein intake was associated with higher BMD in premenopausal women (10) . No similar

association was observed among postmenopausal women. However, postmenopausal women who reported one or more fractures of the hip, spine, or forearm had significantly lower dietary intakes of protein than postmenopausal women without a history of hip fracture. In an observational study of hospitalized elderly men and women, participants with dietary protein intake greater than 1 g/kg/day had higher BMD of the femoral neck than those with protein intakes less than $1 \frac{g}{kg}$ day (11). Furthermore, women in this study with higher protein intakes had an increased capacity to climb stairs and greater muscle strength than did women consuming lower protein intakes.

Others have studied the relationship between protein intake and bone mineral density in relation to common dietary patterns such as vegetarianism. In a study of postmenopausal vegetarian women in Taiwan, long-term adherents to a strict vegan diet had four times the risk of being classified as having osteopenia of the femoral neck than did those following less strict dietary practices (9). In a survey of elderly Chinese females, BMD at the hip was lower in vegetarians than omnivores, and was positively correlated to protein intake (91).

Recent reports add controversy to the issue of dietary protein intake and relation to BMD. In the Study of Osteoporotic Hip Fractures, women with a high ratio of animal to vegetable protein intake lost bone more rapidly than did those with a low ratio and had an almost four-fold increase in hip fracture risk (12). Contrary to what might have been expected according to the acid-ash hypothesis, participants with the highest ratios of animal to vegetable protein intake had marginally higher BMD of the hip at baseline than did those with lower ratios. Hannan et al. (8) studied a cohort of men and women from the Framingham Heart Study and found lower protein intake was significantly related to

BMD loss at the hip and spine. Possibly influenced by the controversy of animalprotein's harmful effect on bone health fueled by the findings from Sellmeyer et al. (12), Hannan et al. (8) also examined the relationship between animal protein intake and BMD but found no evidence of an adverse effect on bone (92). The effect of animal protein seemed similar to the effect of total protein and lower percent animal protein was related to bone loss at the hip and spine. This finding is consistent with findings from others who report lower BMDs in strict adherers to vegetarian diets as well as a negative association between animal protein intake and risk of hip fracture (9) (16) (91).

Future Directions for Research

Although there is a large and growing body of evidence lending support to dietary protein's role in bone health, even the most recent reports from large-scale observational studies examining this relationship in regard to risk of hip fracture are conflicting (8) (12). Like other diet-disease relationships, the protein-osteoporosis association is complex and additional research is needed to clarify the association. One direction for future research may be in examining interactions between nutritional, genetic, and environmental factors. For example, stratifying analyses by individuals with high-risk alleles for osteoporosis, unidentified in observational studies to-date, may identify groups of people more susceptible to nutritional or environmental causes of hip fracture.

It has already been established that protein intake and calcium balance are interrelated. Some have proposed that while higher dietary protein may indeed increase urinary calcium leading to bone loss, adequate levels of calcium in the presence of higher protein may protect bone. Researchers may find it useful to evaluate diets on their

calcium-to-protein ratios rather than crude or adjusted protein intake alone. Other nutrient-nutrient interactions, such as protein and phosphorous, may also be important.

Future research may also focus on examining relationships between protein intake and bone health by food source and food group. Both controlled trials and observational studies have identified differences between protein of animal and vegetable origin in relation to bone health. Some have proposed that the sulfur-containing amino acid content of animal proteins increases acid-ash in the body and is responsible for the deleterious effects. However, in some observational studies animal protein appears protective (16) (8). Some, but not all, animal proteins produce acid-ash and some vegetable foods are high in sulfur containing amino acids. Analyzing diets based on food groups may allow researchers to identify specific foods, not necessarily designated by animal or vegetable origin, important in the relationship. Possible foods to consider are milk and non-cheese dairy products. Although they are animal protein foods, they do not have a high potential renal acid load and are also good sources of protein and calcium (37).

Another avenue researchers may pursue is examining protein quality and amino acid content of foods in relation to risk of hip fracture. The essential amino acid lysine, for example, is involved in the cross-linking of both collagen and osteopontin (93). Abnormalities in the hydroxylation of lysine residue on bone proteins have been observed in osteoporotic bone tissue (94). People with lysinuric protein intolerance who have defective transport of cationic amino acids including lysine have increased incidence of fractures due to decreased synthesis of matrix proteins (95). Foods high in lysine include meats and corn-based grain products. Examining the relationship between lysine intake

or other markers of protein quality may also help clarify conflicting results of studies examining protein intake and risk of fracture.

Summary and Conclusions

The controversy and debate over the relationship between protein intake and bone health or risk of hip fracture in the elderly may be minimized by recognizing that total diet is much more influential to bone health than is one single nutrient. Although metabolic studies of high purified protein diets generally support the acid-ash osteoporosis hypothesis, many observational studies lend support to the hypothesis that total and animal protein are essential for bone health. The nature of observational studies forces investigators to examine confounders in the relationship between protein intake and risk of fracture such as calcium intake, age, and body mass index; however, many important nutrient-nutrient, nutrient-gene, or nutrient-environment interactions may be overlooked and may also modify the relationship.

Protein is an important component of the bone matrix, and dietary protein may influence bone health and risk of hip fracture in several ways. Protein appears to disrupt calcium balance by increasing urinary calcium loss and may result in decreased BMD. However, nutrients commonly found in high protein foods, such as calcium in dairy products and phosphorous in meats, may blunt this affect.

Current recommendations for protein requirements may not be adequate to meet metabolic needs of the elderly. Many elderly people with hip fracture are protein-deplete, and protein supplementation improves medical outcome after hip fracture. Furthermore,

protein restriction decreases levels of IGF-1, known to be osteotrophic, but proteinrepletion improves levels of IGF-1.

As with any diet-disease relationship, associations between the nutrient variable and outcome variable are less clear in the presence of confounders and interactions inherent in observational studies. Future directions in research pertaining to protein's role in bone health, including examination of source of protein intake by food groups and specific amino acids implicated in bone metabolism, may help to clarify the relationship. However, at this time, higher protein intake from diets of varying food sources, especially in the presence of adequate calcium and phosphorous intake, seems more beneficial than harmful to bone health and thus hip fracture risk in the elderly.

References

- 1. Cooper CM, Melton LJ. Magnitude and impact of osteoporosis and fractures. In: Marcus R, ed. Osteoporosis. Washington, DC: Academic Press, Inc., 1996:419- 509.
- 2. Cumming RG, Nevitt MC, Cummings SR. Epidemiology of hip fractures. Epidemiol Rev 1997;19:244-57.
- 3. Cummings SR, Black DM, Rubin SM. Lifetime risks of hip, Calles', or vertebral fracture and coronary heart disease among white postmenopausal women. Arch Intern Med 1989; 149:2445-8.
- 4. Cooper C. The crippling consequences of fractures and their impact on quality of life. Am J Med 1997;103:12S-19S.
- 5. Lindsay R. The burden of osteoporosis: cost. Am J Med 1995;98:9S-11S.
- 6. Deal CL. Osteoporosis: prevention, diagnosis, and management. Am J Med 1997; I 02:35S-39S.
- 7. Ilich JZ, Kerstetter JE. Nutrition in bone health revisited: a story beyond calcium. JAm Coll Nutr 2000;19:715-37.
- 8. Hannan MT, Tucker KL, Dawson-Hughes B, Cupples LA, Felson DT, Kiel DP. Effect of dietary protein on bone loss in elderly men and women: the Framingham Osteoporosis Study. J Bone Miner Res 2000; 15:2504-I2.
- 9. Chiu JF, Lan SJ, Yang CY. Long-term vegetarian diet and bone mineral density in postmenopausal Taiwanese women. Calcif Tissue Int 1997;60:245-9.
- 10. Cooper C, Atkinson EJ, Hensrud DD. Dietary protein intake and bone mass in women. Calcif Tissue Int 1996;58:320-5.
- II. Geinoz G, Rapin CH, Rizzoli R, et al. Relationship between bone mineral density and dietary intakes in the elderly. Osteoporos Int I993;3:242-8.
- I2. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Am J Clin Nutr 2001;73:118-22.
- I3. Meyer HE, Pedersen JI, Loken EB, Tverdal A. Dietary factors and the incidence of hip fracture in middle-aged Norwegians. A prospective study. Am J Epidemiol I997;145:1I7-23.
- I4. Feskanich D, Willett WC, Stampfer MJ, Colditz GA. Protein consumption and bone fractures in women. Am J Epidemiol 1996; I43:472-9.
- 15. Abelow BJ, Holford TR, Insogna KL. Cross-cultural association between dietary animal protein and hip fracture: a hypothesis. Calcif Tissue Int 1992;50: I4-8.
- 16. Munger RG, Cerhan JR, Chiu BC. Prospective study of dietary protein intake and risk of hip fracture in postmenopausal women. Am J Clin Nutr 1999;69:147-52.
- 17. McCance RA, Widdowson EM, and Lehmann H. The effect of protein intake on the absorption of calcium and magnesium. Biochemistry Journal 1942;36:686- 689.
- 18. Wachman A, Bernstein DS. Diet and osteoporosis. Lancet 1968;1 :958-9.
- 19. Johnson NE, Alcantara EN, Linkswiler H. Effect of level of protein intake on urinary and fecal calcium and calcium retention of young adult males. J Nutr 1970; 100:1425-30.
- 20. Walker RM, Linkswiler HM. Calcium retention in the adult human male as affected by protein intake. J Nutr 1972; 102:1297-302.
- 21. Anand CR, Linkswiler HM. Effect of protein intake on calcium balance of young men given 500 mg calcium daily. J Nutr 1974; 104:695-700.
- 22. Heaney RP, Recker RR. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. J Lab Clin Med 1982;99:46-55 .
- 23. Heaney RP. Excess dietary protein may not adversely affect bone. J Nutr 1998;128:1054-7.
- 24. Allen LH, Oddoye EA, Margen S. Protein-induced hypercalciuria: a longer term study. Am J Clin Nutr 1979;32:741-9.
- 25. Licata AA, Bou E, Bartter FC, West F. Acute effects of dietary protein on calcium metabolism in patients with osteoporosis. J Gerontol 1981;36:14-9.
- 26. Itoh R, Nishiyama N, Suyama Y. Dietary protein intake and urinary excretion of calcium: a cross-sectional study in a healthy Japanese population. Am J Clin Nutr 1998;67:438-44.
- 27. Spencer H, Kramer L, Osis D, Norris C. Effect of a high protein (meat) intake on calcium metabolism in man. Am J Clin Nutr 1978;31 :2167-80.
- 28. Spencer H, Kramer L, DeBartolo M, Norris C, Osis D. Further studies of the effect of a high protein diet as meat on calcium metabolism. Am J Clin Nutr 1983;37:924-9.
- 29. Pannemans DL, Schaafsma G, Westerterp KR. Calcium excretion, apparent calcium absorption and calcium balance in young and elderly subjects: influence of protein intake. Br J Nutr 1997;77:721-9.
- 30. Moriguti JC, Ferriolli E, Marchini JS. Urinary calcium loss in elderly men on a vegetable: animal (1:1) high-protein diet. Gerontology 1999; 45:274-8.
- 31. Hunt JR, Gallagher SK, Johnson LK, Lykken GI. High- versus low-meat diets: effects on zinc absorption, iron status, and calcium, copper, iron, magnesium, manganese, nitrogen, phosphorus, and zinc balance in postmenopausal women. Am J Clin Nutr 1995;62 :621-32.
- 32. Whiting SJ, Draper HH. The role of sulfate in the calciuria of high protein diets in adult rats. J Nutr 1980;110:212-22.
- 33. Yuen DE, Draper HH. Long-term effects of excess protein and phosphorus on bone homeostasis in adult mice. J Nutr 1983;113:1374-80.
- 34. Petito SL, Evans JL. Calcium status of the growing rat as affected by diet acidity from ammonium chloride, phosphate and protein. J Nutr 1984;114:1049-59.
- 35. Trilok G, Draper HH. Effect of a high protein intake on acid-base balance in adult rats. CalcifTissue Int 1989;44:339-42.
- 36. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC, Jr. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. N Engl J Med 1994;330:1776-81.
- 3 7. Barzel US, Massey LK. Excess dietary protein can adversely affect bone. J Nutr 1998;128:1051-3.
- 38. Zemel MB, Schuette SA, Hegsted M, Linkswiler HM. Role ofthe sulfurcontaining amino acids in protein-induced hypercalciuria in men. J Nutr 1981 ;111:545-52.
- 39. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Eng! J Med 1997;336: 1117-24.
- 40. Chu JY, Margen S, Costa FM. Studies in calcium metabolism. II. Effects oflow calcium and variable protein intake on human calcium metabolism. Am J Clin Nutr 1975;28: 1028-35.
- 41 . Kerstetter JE, Allen LH. Protein intake and calcium homeostasis. Adv Nutr Res 1994;9: 167-81.
- 42. Schuette SA, Zemel MB, Linkswiler HM. Studies on the mechanism of proteininduced hypercalciuria in older men and women. J Nutr 1980; 110:305-15.
- 43 . Heaney RP. Dietary protein and phosphorus do not affect calcium absorption. Am J Clin Nutr 2000;72:758-61.
- 44. Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. Bone gain in young adult women. JAMA 1992;268:2403-8.
- 45. Massey LK. Does excess dietary protein adversely affect bone? Symposium overview. J Nutr 1998; 128:1048-50.
- 46. Kim Y, Linkswiler HM. Effect of level of protein intake on calcium metabolism and on parathyroid and renal function in the adult human male. J Nutr 1979; 109:1399-404.
- 47. Hegsted M, Schuette SA, Zemel MB, Linkswiler HM. Urinary calcium and calcium balance in young men as affected by level of protein and phosphorus intake. J Nutr 1981; 111 :553-62.
- 48. Heaney RP. Age considerations in nutrient needs for bone health: older adults. J Am Coli Nutr 1996;15:575-8.
- 49. Wilson MM, Vaswani S, Liu D, Morley JE, Miller DK. Prevalence and causes of undernutrition in medical outpatients. Am J Med 1998; 104:56-63.
- 50. Sullivan D, Lipschitz D. Evaluating and treating nutritional problems in older patients. Clin Geriatr Med 1997;13:753-68.
- 51. Bonjour JP, Schurch MA, Rizzoli R. Nutritional aspects ofhip fractures. Bone 1996;18: 139S-144S.
- 52. Tkatch L, Rapin CH, Rizzoli R, et al. Benefits of oral protein supplementation in elderly patients with fracture of the proximal femur. JAm Coli Nutr 1992; 11:519- 25.
- 53. Jensen JE, Jensen TG, Smith TK, Johnston DA, Dudrick SJ. Nutrition in orthopaedic surgery. J Bone Joint Surg [Am] 1982;64: 1263-72.
- 54. Bachrach-Lindstrom M, Unosson M, Ek AC, Arnqvist HJ. Assessment of nutritional status using biochemical and anthropometric variables in a nutritional intervention study of women with hip fracture. Clin Nutr 2001;20:217-23.
- 55 . Patterson BM, Cornell CN, Carbone B, Levine B, Chapman D. Protein depletion and metabolic stress in elderly patients who have a fracture of the hip. J Bone Joint Surg [Am] 1992;74:251-60.
- 56. Hanger HC, Smart EJ, Merrilees MJ, Frampton CM. The prevalence of malnutrition in elderly hip fracture patients. N Z Med J 1999;112:88-90.
- 57. Panzer S, Tidermark J, Brismar K, Aderqvist S, Cederholm T. Nutritional status, insulin-like growth factor-1 and quality of life in elderly women with hip fractures. Clin Nutr 1999;18:241-246.
- 58. Bonjour JP, Schurch MA, Rizzoli R. Proteins and bone health. Pathol Bioi (Paris) 1997;45:57-9.
- 59. Foster MR, Heppenstall RB, Friedenberg ZB, Hozack WJ. A prospective assessment of nutritional status and complications in patients with fractures of the hip. J Orthop Trauma 1990;4:49-57.
- 60. Dreblow DM, Anderson CF, Moxness K. Nutritional assessment of orthopedic patients. Mayo Clin Proc 1981;56:51-4.
- 61 . Bastow MD, Rawlings J, Allison SP. Undernutrition, hypothermia, and injury in elderly women with fractured femur: an injury response to altered metabolism? Lancet 1983; 1:143-6.
- 62. Orwoll ES. The effects of dietary protein insufficiency and excess on skeletal health. Bone 1992; 13:343-50.
- 63. Bourrin S, Toromanoff A, Ammann P, Bonjour JP, Rizzoli R. Dietary protein deficiency induces osteoporosis in aged male rats. J Bone Miner Res 2000;15:1555-63.
- 64. Heaney RP. Nutritional factors in osteoporosis. Annu Rev Nutr 1993; 13:287-316.
- 65. Schurch MA, Rizzoli R, Slosman D, Vadas L, Vergnaud P, Bonjour JP. Protein supplements increase serum insulin-like growth factor-I levels and attenuate proximal femur bone loss in patients with recent hip fracture. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 1998; 128:801-9.
- 66. National Research Council. Recommended dietary allowances. 1Oth ed. Washington, DC: National Academy Press, 1989.
- 67. Kurpad AV, Vaz M. Protein and amino acid requirements in the elderly. Eur J Clin Nutr 2000;54:Sl31-S142.
- 68. Zanni E, Calloway DH, Zezulka A Y. Protein requirements of elderly men. J Nutr 1979; I 09:513-24.
- 69. Cheng AH, Gomez A, Bergan JG, Lee TC, Monckeberg F, Chichester CO. Comparative nitrogen balance study between young and aged adults using three levels of protein intake from a combination wheat-soy-milk mixture. Am J Clin Nutr 1978;31:12-22.
- 70. Gersovitz M, Motil K, Munro HN, Scrimshaw NS, Young VR. Human protein requirements: assessment of the adequacy of the current Recommended Dietary Allowance for dietary protein in elderly men and women. Am J Clin Nutr 1982;35 :6-14.
- 71. U auy R, Scrimshaw NS, Young VR. Human protein requirements: nitrogen balance response to graded levels of egg protein in elderly men and women. Am J Clin Nutr 1978;31 :779-85.
- 72. Campbell WW, Evans WJ. Protein requirements of elderly people. Eur J Clin Nutr 1996;50 Suppl 1:S180-185.
- 73 . Campbell WW, Crim MC, Dallal GE, Young VR, Evans WJ. Increased protein requirements in elderly people: new data and retrospective reassessments. Am J Clin Nutr 1994;60:501-9.
- 74. Porter KH, Johnson MA. Dietary protein supplementation and recovery from femoral fracture. Nutr Rev 1998;56:337-40.
- 75. Bunker VW, Lawson MS, Stansfield MF, Clayton BE. Nitrogen balance studies in apparently healthy elderly people and those who are housebound. Br J Nutr 1987;57:211-21.
- 76. Castaneda C, Charnley JM, Evans WJ, Crim MC. Elderly women accommodate to a low-protein diet with losses of body cell mass, muscle function, and immune response. Am J Clin Nutr 1995;62:30-9.
- 77. Young VR, Borgonha S. Nitrogen and amino acid requirements: the Massachusetts Institute of Technology amino acid requirement pattern. J Nutr 2000;130:1841S-9S.
- 78 . Munro HN, McGandy RB, Hartz SC, Russell RM, Jacob RA, Otradovec CL. Protein nutriture of a group of free-living elderly. Am J Clin Nutr 1987;46:586- 92.
- 79. Vellas BJ, Hunt WC, Romero LJ, Koehler KM, Baumgartner RN, Garry PJ. Changes in nutritional status and patterns of morbidity among free-living elderly persons: a 10-year longitudinal study. Nutrition 1997;13:515-9.
- 80. Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. Dietary supplementation in elderly patients with fractured neck of the femur [see comments]. Lancet 1990;335:1013-6.
- 81. Espaulella J, Guyer H, Diaz-Escriu F, Mellado-Navas JA, Castells M, Pladevall M. Nutritional supplementation of elderly hip fracture patients. A randomized, double-blind, placebo-controlled trial. Age Ageing 2000;29:425-31 .
- 82. Bonjour JP, Schurch MA, Chevalley T, Ammann P, Rizzoli R. Protein intake, IGF-1 and osteoporosis. Osteoporos Int 1997;7:S36-42.
- 83. Johansson AG, Forslund A, Hambraeus L, Blum WF, Ljunghall S. Growth hormone-dependent insulin-like growth factor binding protein is a major determinant of bone mineral density in healthy men. J Bone Miner Res 1994;9:915-21.
- 84. Canalis E, McCarthy TL, Centrella M. Growth factors and cytokines in bone cell metabolism. Annu Rev Med 1991 ;42:17-24.
- 85. Castaneda C, Gordon PL, Fielding RA, Evans WJ, Crim MC. Marginal protein intake results in reduced plasma IGF-1 levels and skeletal muscle fiber atrophy in elderly women. J Nutr Health Aging 2000;4:85-90.
- 86. Campillo B, Paillaud E, Bories PN, Noel M, Porquet D, Le Parco JC. Serum levels of insulin-like growth factor-1 in the three months following surgery for a

hip fracture in elderly: relationship with nutritional status and inflammatory reaction. Clin Nutr 2000; 19:349-54.

- 87. Bourrin S, Ammann P, Bonjour JP, Rizzoli R. Dietary protein restriction lowers plasma insulin-like growth factor I (IGF-I), impairs cortical bone formation, and induces osteoblastic resistance to IGF-I in adult female rats [In process citation]. Endocrinology 2000; 141 :3149-55.
- 88. Ammann P, Bourrin S, Bonjour JP, Meyer JM, Rizzoli R. Protein undernutritioninduced bone loss is associated with decreased IGF-I levels and estrogen deficiency. J Bone Miner Res 2000; 15:683-90.
- 89. Friedlander AL, Butterfield GE, Moynihan S, et al. One year of insulin-like growth factor I treatment does not affect bone density, body composition, or psychological measures in postmenopausal women. J Clin Endocrinol Metab 2001 ;86: 1496-503.
- 90. Frassetto LA, Todd KM, Morris RC, Jr. , Sebastian A. Worldwide incidence of hip fracture in elderly women: relation to consumption of animal and vegetable foods. J Gerontal A Bioi Sci Med Sci 2000;55:M585-92.
- 91. Lau EM, Kwok T, Woo J, Ho SC. Bone mineral density in Chinese elderly female vegetarians, vegans, !acto-vegetarians and omnivores. Eur J Clin Nutr 1998;52:60-4.
- 92. Heaney RP. Protein intake and bone health: the influence of belief systems on the conduct of nutritional science. Am J Clin Nutr 2001;73:5-6.
- 93. Knott L, Bailey AJ. Collagen cross-links in mineralizing tissues: a review of their chemistry, function, and clinical relevance. Bone 1998;22: 181-7.
- 94. Bailey AJ, Wotton SF, Sims TJ, Thompson PW. Post-translational modifications in the collagen of human osteoporotic femoral head. Biochem Biophys Res Commun 1992;185:801-5.
- 95. Parto K, Penttinen R, Paronen I, Pelliniemi **L,** Simell 0. Osteoporosis **in** lysinuric protein intolerance. J Inherit Metab Dis 1993;16:441-50.

CHAPTER 4

PROTEIN INTAKE AND RISK OF OSTEOPOROTIC HIP FRACTURE IN ELDERLY RESIDENTS OF UTAH³

Abstract

Protein is an important component of bone, but the role of dietary protein intake in osteoporosis and fracture risk remains controversial. The role of dietary protein intake in osteoporotic hip fracture was evaluated in a statewide case-control study in Utah. Patients with hip fracture aged 50- 89 years (cases) were ascertained via surveillance of 18 Utah hospitals during 1997- 2001. Age- and gender-matched controls were randomly selected. Participants were interviewed in their residence, and diet was assessed using a picture-sort food frequency questionnaire. Risk of hip fracture was evaluated by quartile of protein intake and stratified by age-group for 792 cases (570 women, 222 men) and 1104 controls (703 women, 401 men). In analyses that controlled for gender, estrogen use, body mass index, smoking status, alcohol use, energy and calcium intake, and physical activity, the risk of hip fracture decreased across increasing quartiles of total protein intake for participants aged 50- 69 years (OR: 1.0 (reference); 0.38 (95% CI: 0.21 - 0.71); 0.59 (0.32 - 1.10); 0.22 (0.11 - 0.45); p for trend = < 0.001). No similar associations were observed among older participants. Higher total protein intake was associated with a reduced risk of hip fracture in men and women aged 50- 69 years and did not appear to increase risk of hip fracture in men and women aged 70- 89 years. The

³Coauthored by Heidi J. Wengreen, Ronald G. Munger, Nancy A. West, D. Richard Cutler, Christopher D. Corcoran, Jianjun Zhang, and Nancy E. Sassano.

effect of dietary protein intake on risk of hip fracture may be modified by age, and this may account for the conflicting results of previous studies.

Introduction

Bone fractures due to osteoporosis have long plagued the elderly of industrialized countries and are now an emerging problem in developing countries (1). Hip fractures are the most serious of all fractures related to osteoporosis (2). Although the incidence of hip fracture is higher in women than in men, rates increase exponentially with age in both and the age-specific rates in men lag those of women by only five to seven years (2-3). The lifetime risk of suffering a hip fracture is 6.0% in Caucasian men and 17.5% in Caucasian women (4). One year after hip fracture, 40% of patients cannot walk alone, 60% have difficulty with at least one essential activity of daily living, 27% have been admitted to a nursing home for the first time, and 20% have died (5). Discovering new methods for the prevention of osteoporotic hip fractures will decrease this burden and may help many elders remain independent and have a higher quality of life in their later years.

Osteoporosis is characterized by low bone mass and microarchitectural deterioration of bone tissue resulting in increased bone fragility and susceptibility to fracture (6). Although peak bone mass has a significant genetic component, modifiable risk factors, including nutrition, appear to play an important role in bone health throughout the life-cycle. Dietary interventions for the prevention and treatment of osteoporosis have long been focused on calcium, phosphorous, and vitamin D while other nutrients, including protein, have been less well studied.

Protein is an important component of bone (7) and protein supplementation improves the medical outcome in elderly hip fracture patients (8-9), but the role of dietary protein intake in osteoporotic hip fractures remains controversial. Although several population-based observational studies have examined the relationship between dietary protein intake and risk of hip fracture, their results are conflicting (10-12) (13). Therefore, the association between dietary protein intake and risk of osteoporotic hip fracture was examined in a statewide case control study of older Utah residents. The effects of animal protein and vegetable protein were also examined.

Subjects and Methods

The Utah Study of Nutrition and Bone Health (USNBH) is a statewide casecontrol study of risk factors of hip fracture in Utah residents aged 50- 89 years. Cases were ascertained via surveillance of 18 Utah hospitals responsible for treating 98% of hip fracture cases in the state. Controls were randomly selected from the Utah Drivers License and Medicare databases and frequency-matched to cases by gender and 5-year age intervals. All study procedures were reviewed and approved by the institutional review board of each hospital and participating university. After obtaining written informed consent, an in-person interview was conducted at each participant's place of residence.

The percentage of subjects who refused to complete an interview was similar for cases and controls (23. 7% and 24.1 %, respectively); however, more cases than controls were too frail, ill, or demented to complete the interview (21.9% and 9.9%, respectively) or died before the interview could be completed (14.4% and 5.7%, respectively). An

additional 2.6% of cases and 2.5% of controls could not be located. As a result, the overall participation rate was 37.5% for cases ($n = 818$) and 57.8% for controls ($n =$ 1142).

Data Collection

Diet was assessed using a 137-item picture-sort food frequency questionnaire (FFQ). The Utah picture-sort FFQ was developed specifically for this population as an alternative to the more traditional paper-and-pencil format FFQ. Foods included in the Utah picture-sort FFQ were systematically selected from the 126-item Nurses' Health Study FFQ, the National Cancer Institute (NCI) FFQ, and a list of commonly eaten foods as identified in focus groups of elderly in Utah. The picture-sort FFQ method, first developed by Kumanyika et al. (14), engages respondents by having them sort cards with color photographs of foods into trays representing frequency of use over the past year (for controls) or the year before hip fracture (for cases). An interviewer records information about specific consumption patterns for foods within each frequency category. The picture-sort FFQ was found to be reproducible on repeated administration and accurate compared with dietary recall interviews (15). FFQ data were converted to usual daily intakes by transforming all consumption periods to consumption per day and multiplying by frequency of use and weight of the standard serving size. Respondents with implausible total energy intake $(< 600 \text{ or } > 5000 \text{ calories})$ were excluded from the analyses $(n = 31)$.

A detailed history of vitamin and mineral supplementation use was obtained during the interview. Daily calcium intake from individual, combination, or multivitamin

and mineral supplements was combined with dietary calcium intake to give a measure of total daily calcium intake in milligrams.

Other characteristics assessed and included as covariates in the analyses were total energy intake, gender, weight, height, Mini-Mental State Examination (MMSE), smoking status, alcohol use, physical activity level and, in women, estrogen use. Selfreported measures of weight and height were used to compute body mass index (kg/m²). The MMSE was scored and adjusted for sensory impairment to give a measure of cognitive ability. Respondents with an adjusted MMSE score of 17 or less, indicating severe cognitive impairment (16), were excluded from the analyses $(n = 21)$. Hip fractures caused by high-impact trauma (such as motor vehicle accident or a fall from the roof of a house) were also excluded ($n = 77$). Smoking status was characterized as current smoker (smoked regularly in past year or year before hip fracture), former smoker, or never smoked. Similarly, alcohol use was characterized as current user (regularly drank one or more drinks per month over the past year or year before hip fracture), former user, or never user. Recent physical activity was classified by hours per week for a number of recreational and household activities and then categorized into four levels. Women were categorized into current users, former users, or never users of estrogen.

Statistical Analyses

Dietary intakes were analyzed by using nutrient food composition data from the Food Processor dietary assessment program (Food Processor Nutrition Analyses & Fitness Software, Version 7.1 , ESHA Research, Salem, OR), USDA food composition tables (www.nal. usda.gov/fnic/foodcomp/Data/index.html), and product information from manufacturers. To quantify protein intake in relation to total caloric intake, protein

was expressed as a percentage of total energy intake (protein % E). Quartiles of total protein % E, animal protein % E, and vegetable protein % E for all participants were used to define levels of exposure. In order to compare methods, Willet and Stampfer's (17) residual method for energy adjustment was also applied and produced similar results to those presented here.

Logistic regression models were used to evaluate the relationships between the dietary protein variables and risk of hip fracture. Odds ratios were calculated using the lowest nutrient quartile as the reference intake. All combinations of interactions between quartiles of protein intake, age, and gender were tested by comparing likelihood-ratio statistics for the logistic regression model with each of three two-way interactions to the model with only the main effects. Of the interactions examined, only the interactions between age and quartile of total protein intake and quartile of animal protein intake were significant (p-value = 0.007 , < 0.0001 respectively). Thus, both men and women were included in the analyses which were then stratified by three age-groups (50 - 69 year olds, 70 - 79 year olds, and 80- 89 year olds). Because animal and vegetable protein intake were not highly correlated $(r = -0.33)$, they were included together in logistic regression models testing the effect of animal and vegetable protein intake on risk of hip fracture. Multivariate logistic regression models were used to control for the possible confounding effects of body mass index, smoking, alcohol use, physical activity level, total calcium intake, and in women, estrogen. The linear trends across quartiles of protein intake were tested by weighting each quartile by its median value. All analyses were performed with SPSS software, version 10.0 and SAS software, version 8.

Results

Data on age, anthropometric, nutrition, and lifestyle characteristics for 623 male participants (401 controls, 222 cases) and 1273 female participants (703 controls, 570 cases) are shown in Table 4-1. Participants with hip fracture were older ($p = 0.001$), weighed less ($p < 0.001$), and had a lower mean body mass index ($p < 0.001$) than participants without hip fracture. Seventy-two percent of cases and 64% of controls were female. Although cases consumed more total calories than controls ($p = 0.011$), controls consumed a larger percentage of total calories from protein ($p = 0.006$). The mean physical activity reported per week and the mean total dietary calcium did not differ significantly between cases and controls for men or women. In women, more cases than controls reported being current smokers ($p = 0.023$); there were no differences in smoking status between male cases and controls. There were no significant differences in regular alcohol use between groups although more men reported regularly consuming alcohol than women. Among women, more controls than cases reported currently using an estrogen supplement ($p < 0.001$).

The percentage of contribution to total dietary protein intake by food group for cases and controls is shown in Table 4-2. The red meat (beef, pork, lamb, venison), dairy, and bread and cereal food groups contributed more than 50% of total dietary protein intake in cases and controls of both genders.

Mean intake of protein $\%$ E was similar for male and female cases (15.5%) and for male and female controls (15.8%). A decline in total protein intake with increasing age was generally observed for both men and women (Figure 4-1). In men, mean protein % E was 16.0% in 50-69 year olds, 15.8% in 70-79 year olds, and 15.3% in 80-89

Characteristics of 793 cases and 1105 controls by gender; Utah Study of Nutrition and Bone Health

 $¹$ Means \pm SD.</sup>

 2 Protein as a percent of total energy intake.

Table 4-2

Percentage contribution of food groups to total dietary protein intake by case- control status and gender; the Utah Study of Nutrition and Bone Health

 \top Other group includes supplemental beverages, soups, butter, margarine, and many snack and dessert type foods.

Figure 4-1. Mean total protein intake as a percent of total energy (% E) of cases and controls by sex and by age-group; the Utah Study of Nutrition and Bone Health.

year olds. Similarly, in women, mean protein $\%$ E was 16.0 $\%$ in 50 - 69 year olds, 15.6% in 70- 79 year olds, and 15.4% in 80- 89 year olds. Within each age-group, cases generally had a lower mean protein intake compared to controls, and this difference was most striking in the youngest age-group (50- 69 year olds). In men, controls aged 50- 69 years consumed 16.9% of energy from protein and cases consumed 15.5% of energy from protein. In women, controls aged 50 - 69 years consumed 16.3% of energy from protein and cases consumed 15.4% of energy from protein. The differences in protein % E between cases and controls were much smaller in participants aged 70- 89 years and 80- 89 years than were the differences between cases and controls aged 50- 69 years.

In logistic regression models that controlled for gender and interactions between age, gender, and protein intake, the risk of hip fracture decreased with increasing quartile of percent total protein intake for participants aged 50 - 69 years (OR: 1.0 (reference); 0.40 (95% confidence interval (CI) 0.22- 0.99); 0.51 (95% CI 0.28- 0.91); 0.22 (95% CI $0.11 - 0.44$) p-trend: ≤ 0.0001 ; no similar associations were observed among older participants (70 - 89 year olds). Major risk factors for hip fracture including body mass index, smoking status, alcohol use, physical activity, calcium intake, and in women, estrogen use were examined in multivariate analyses. Odds ratios for risk of hip fracture reported by age-group across increasing quartiles of percent protein intake adjusting for these additional potential confounders are shown in Table 4-3. Including these additional variables in the model did not change the association between protein intake and risk of hip fracture observed in the unadjusted analyses. The risk of hip fracture also decreased across increasing quartiles of total protein intake for participants aged 50-69 years in the adjusted analyses (OR: I (reference); 0.38 (95% CI 0.21 - 0.71); 0.59 (95% CI 0.32-

Table 4-3

Multivariate adjusted odds ratios for risk of hip fracture in Utah men and women by quartile of percent energy provided by total protein (protein % E), stratified by agegroup; the Utah Study of Nutrition and Bone Health

¹ Multiple logistic regression models controlled for the effects of gender, body mass index, smoking status, alcohol use, physical activity, calcium intake, and estrogen use in women.

² Linear trend across quartile of protein intake with the median value per quartile.

³ Multiple logistic regression models controlled for the effect of vegetable protein and other variables described in the total protein analyses.

⁴ Multiple logistic regression models controlled for the effect of animal protein and other variables described in the total protein analyses.

1.10); 0.22 (95% CI 0.11 - 0.45) p-trend = 0.002); no similar association was observed among older participants (aged 70- 89 years). Significant protective effects of protein consumption in the highest vs. lowest quartile of intake were seen for total protein (OR: 0.22, 95% CI 0.11 - 0.45), animal protein (OR: 0.23, 95% CI 0.11 - 0.51), and vegetable protein (OR: 0.49 , 95% CI $0.24 - 1.00$) in participants aged $50 - 69$ years, suggesting that both animal and vegetable protein contribute to the association.

Although odds ratios for risk of hip fracture by increasing quartile of total protein intake indicated no apparent association with risk of hip fracture in participants aged 70 - 79 years and 80 - 89 years, the association between animal and vegetable protein intake and risk of hip fracture is less clear.

Discussion

Total protein intake was inversely associated with risk of hip fracture in Utah men and women aged 50 - 69 years. Both animal and vegetable sources of protein contributed to this association. For participants aged 50- 69 years the risk of hip fracture in the highest quartile of protein intake was 78% less than the risk at the lowest quartile of intake (OR: 0.22, 95% CI 0.11 - 0.45). Increasing total protein intake was not associated with increased risk of hip fracture in older participants of the Utah study (aged 70 - 89 years), as has been suggested in previous reports (13, 18, 19). Thus, the relationship between dietary protein intake and risk of hip fracture appears to be modified by age. In the Utah population, protein intake generally declined with increasing age in both men and women and cases reported lower protein intake at younger ages than controls. This observation is consistent with findings from studies of other aging populations (13, 20)
and may be important in interpreting the relationship between dietary protein intake and risk of hip fracture in aging populations.

The role of dietary protein in bone health has been controversial. Wachman and Berstein hypothesized in 1968 that diets high in meat and animal protein elevate metabolic acid production and lead to chronic bone buffering and loss (21). Since then, a variety of cross-cultural (22-23), experimental (24-25), and observational (13) (18-19) studies have produced results consistent with this hypothesis. However, others argue that dietary protein intake has a negative effect on bone metabolism only in the presence of low calcium intake and that protein consumption within the normal range of intake together with an adequate calcium intake would be far more protective than harmful in aging populations(26-27).

Several lines of evidence point to the overall positive role of protein intake in bone health. Prevalence of protein energy malnutrition increases with advancing age and is common in older hip fracture patients (6) (28). In clinical trials, an oral protein supplement was found to reduce complications and mortality due to hip fracture in elderly patients (8) (29). Further studies found that protein-containing supplements attenuated proximal femur bone loss and increased serum levels of insulin-like growth factor in patients with recent hip fracture (9). Protein restriction has been shown to reduce plasma levels of insulin-like growth factor, known to be osteotrophic (30).

Our findings in Utah are in agreement with at least two population-based studies reporting positive effects of increased protein intake on bone health. In the Iowa Women's Health Study, Munger et al. (II) reported that women with higher intakes of total protein and animal protein had a lower risk of hip fracture than women with lower

intakes. The average age of participants in the Iowa Women's Health study was 61-63 years, similar to that of participants in the youngest age group in the Utah study (50-69 year olds). More recently, Hannan et al. (12) reported that men and women in the Framingham Study in the lowest quartile of protein intake had a greater amount of bone loss than women in the highest quartile. In addition, animal protein intake did not appear to adversely affect bone mineral density in this population. The average age of participants in the Framingham study was 74.5 years (range: 68- 91), slightly older than the mean age of participants in the Utah study.

Participants in the Utah study had a mean protein % E consumption of 15.7%, which is greater than that suggested by the current recommended daily allowance (RDA) but similar to reported values from other elderly populations (12) (20) (31). Approximately 18% of the Utah participants had dietary protein intakes less than the current RDA of 0.8 g/kg, which equates to approximately 10.5% of total energy from protein. The majority of total protein intake in the Utah population was derived from animal sources (64%). However, this ratio of animal to vegetable protein was lower than reported elsewhere (11) (13) (31) .

The discrepant findings in risk of hip fracture for participants 50 - 69 years of age compared with older participants (70- 89 years of age) across increasing quartiles of dietary protein intake have several possible explanations. Biological differences in bone loss or factors affecting bone loss experienced by younger participants and older participants may be responsible for the age-modification of risk of hip fracture across increasing protein intake. For example, in women, early bone loss in the years directly following menopause may be related to increased osteoclast activity due to estrogen

withdrawal, whereas bone loss experienced at later ages is most likely due to both a decrease in osteoblast and an increase in osteoclast activity (32).

Protein is an important component of the bone matrix. In addition, adequate dietary protein intake helps improve muscle strength and movement coordination, provides protection around bones, and may consequently decrease a person's propensity to suffer a fracture due to a fall (9, 33). Insulin-like growth factor (IGF), known to be osteotrophic, decreases with age and with low protein diets (30). Increasing dietary protein intake during the sixth and seventh decades may help to decrease risk of hip fracture because other risk factors for fracture are less prevalent than in later years. In later years, elderly are likely to have a lower level of physical activity than in previous years, muscle mass and protective soft tissue padding decrease, and propensity to fall increases (34-35). Low dietary protein intake may accelerate these changes, but they may likely occur despite adequate dietary protein intake. Thus, because other risk factors for hip fracture increase with age, higher protein intake may appear to be less protective in older subjects. Other factors associated with bone loss, such as vitamin D status, sexhormone levels, renal function, and calcium homeostasis (36), may also modify protein's protective effect on bones throughout the life-span.

Lower levels of exposure to protein intake reported by both cases and controls at older ages may have also attenuated the relationship between dietary protein intake and risk of hip fracture in older participants on the statistical grounds of reduced power. Our data as well as other data (20) suggest that protein intake expressed as a percent of total calories decreases as people age. Sellmeyer et al. (13) reported that women with higher ratios of animal to vegetable protein intake were younger than women with lower ratios.

Factors affecting protein intake may be influenced by age and include changes in socioeconomic status, taste, appetite, and the ability to cut and chew meat.

A beneficial effect of dietary protein on risk of hip fracture may exist in older participants but may have been difficult to detect due to limitations of the dietary assessment method. In the Utah study we used a semi-quantitative picture-sort food frequency questionnaire to assess usual dietary intake. As with other semi-quantitative food frequency questionnaires, this method ranks individuals according to usual nutrient intake. While this method is quick and relatively easy to administer and therefore popular in large population-based studies, it lacks the precision of methods designed to capture exact dietary intake on a few days such as multiple weighed diet records or 24-hour recalls (37). In a validation study that compared mean nutrient intakes reported from the Utah picture-sort FFQ to mean nutrient intakes reported from the average of three 24 hour dietary recalls, women 70 years of age or older had lower correlations between methods for protein intake than did younger women or men (15). Physical and cognitive limitations that occur naturally with increasing age may hinder elderly participants' ability to accurately report nutrient intakes using the picture-sort FFQ or other dietary assessment methods. Limitations of the FFQ in elderly populations may increase measurement error and may attenuate diet-disease relationships.

A fourth explanation for the discrepant findings may be the difficulty in obtaining information from participants in the older age groups. While the refusal rates were similar for younger participants aged 50 - 69 years and older participants aged 70 - 89 years (23%), the rates of interview completion were higher for younger participants (59%) than older participants (40%). Older participants were more likely to die before the interview

could be conducted (12%) and more likely to be unable to complete the interview due to frailty, illness, or dementia $(18%)$ than where younger participants $(4\%, 6\%,$ respectively). Herzog et al. (38) found that response rates decline linearly with increasing age in large interview surveys. Inherent difficulties encountered in observational studies of the oldest old make it difficult to generalize results to include this segment of the population. Results from age-stratified data representing people in these oldest age groups may be biased such that the conclusions over or underestimate the diet-disease relationship.

We acknowledge several limitations of the Utah study. Recall bias is always an issue in case-control studies because information that is self-reported after the fact of a hip fracture may be biased and consequently distort results. Elderly people may be more likely to misreport information due to problems associated with aging such as memory loss, poor cognition, and hearing or visual impairments that affect their ability to respond to the interview. Finally, 16.2% of the participants were too frail or ill to complete our interview, and 10.3% died before an interview could be completed. Therefore, our population of older Utah residents may be healthier or in other ways different than the general population of the same age range and findings should be interpreted cautiously.

In conclusion, dietary protein intake was inversely associated with a risk of hip fracture in Utah residents aged 50 - 69 years. Although not protective, higher total dietary protein intake did not appear to increase risk of hip fracture in the oldest participants aged 70 - 89 years. The Utah findings support the view that dietary protein intake appears to be more beneficial than harmful in the elderly who are at risk for bone fractures due to osteoporosis. The effect modification of age on the relationship between protein intake

and risk of hip fracture may in part explain the conflicting findings of previous studies. Modification of protein intake late in life may help to decrease the burden of osteoporosis and thus enhance the quality of life for the rapidly growing population of elderly persons. To better understand this relationship, sources of protein intake including animal versus vegetable origin, specific foods and food groups, and the role of specific amino acids should be explored. Investigators examining these relationships in other populations should also consider how age modifies dietary protein intake and the relationship between protein intake and risk of osteoporotic fractures.

References

- 1. Melton LJ. Hip fractures: a worldwide problem today and tomorrow. Bone 1993;14:S1-8.
- 2. Cumming RG, Nevitt MC, Cummings SR. Epidemiology of hip fractures. Epidemiol Rev 1997; 19:244-57.
- 3. Riggs BL, Melton LJ. The prevention and treatment of osteoporosis [published erratum appears in N Engl J Med 1993 Jan 7;328(1):65]. N Engl J Med 1992;327:620-7.
- 4. Cooper CM, L.J. Magnitude and impact of osteoporosis and fractures. In: Marcus R, ed. Osteoporosis. Academic Press, Inc., 1996:419-509.
- 5. Cooper C. The crippling consequences of fractures and their impact on quality of life. Am J Med 1997;103:12S-17S; discussion 17S-19S.
- 6. Bonjour JP, Schurch MA, Rizzoli R. Nutritional aspects of hip fractures. Bone 1996; 18: 139S-144S.
- 7. Wildman REC, Medeiros DM, Advanced human nutrition. Boca Raton: CRC Press LLC, 2000.
- 8. Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. Dietary supplementation in elderly patients with fractured neck of the femur [see comments]. Lancet 1990;335:1013-6.
- 9. Schurch MA, Rizzoli R, Slosman D, Vadas L, Vergnaud P, Bonjour JP. Protein supplements increase serum insulin-like growth factor-I levels and attenuate proximal femur bone loss in patients with recent hip fracture. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 1998; 128:801-9.
- 10. Feskanich D, Willett WC, Stampfer MJ, Colditz GA. Protein consumption and bone fractures in women. Am J Epidemiol 1996;143:472-9.
- 11. Munger RG, Cerhan JR, Chiu BC. Prospective study of dietary protein intake and risk ofhip fracture in postmenopausal women. Am J Clin Nutr 1999;69:147-52.
- 12. Hannan MT, Tucker KL, Dawson-Hughes B, Cupples LA, Felson DT, Kiel DP. Effect of dietary protein on bone loss in elderly men and women: the Framingham Osteoporosis Study.[In Process Citation]. J Bone Miner Res 2000;15:2504-12.
- 13. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Am J Clin Nutr 2001;73:118-22.
- 14. Kumanyika S, Tell GS, Fried L, Martel JK, Chinchilli VM. Picture-sort method for administering a food frequency questionnaire to older adults. J Am Diet Assoc 1996;96:137-44.
- 15. Wengreen H. Comparison of a picture-sort food frequency questionnaire with 24 hour dietary recalls in an elderly Utah population. Public Health Nutr 2001;4:961- 970.
- 16. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA 1993;269:2386-91.
- 17. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986; 124:17-27.
- 18. Itoh R, Nishiyama N, Suyama Y. Dietary protein intake and urinary excretion of calcium: a cross- sectional study in a healthy Japanese population. Am J Clin Nutr 1998;67:438-44.
- 19. Meyer HE, Pedersen JI, Loken EB, Tverdal A. Dietary factors and the incidence of hip fracture in middle-aged Norwegians. A prospective study. Am J Epidemiol 1997;145:117-23.
- 20. Block G SE. Estimate of nutrient intake from a food frequency questionnaire: The 1987 National Health Interview Survey. American Dietetic Association 1992;92:969-977.
- 21. Wachman A, Bernstein DS. Diet and osteoporosis. Lancet 1968;1 :958-9.
- 22. Abelow BJ, Holford TR, Insogna KL. Cross-cultural association between dietary animal protein and hip fracture: a hypothesis. Calcif Tissue Int 1992;50:14-8.
- 23. Frassetto LA, Todd KM, Morris RC, Jr., Sebastian A. Worldwide incidence of hip fracture in elderly women: relation to consumption of animal and vegetable foods. J Gerontol A Biol Sci Med Sci 2000;55:M585-92.
- 24. Heaney RP, Recker RR. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. J Lab Clin Med 1982;99:46-55.
- 25. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC, Jr. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. N Engl J Med 1994;330:1776-81.
- 26. Spencer H, Kramer L, Osis D. Do protein and phosphorus cause calcium loss? J Nutr 1988;118:657-60.
- 27. Heaney RP. Excess dietary protein may not adversely affect bone. J Nutr I998; I28: I 054-7.
- 28. Jensen JE, Jensen TG, Smith TK, Johnston DA, Dudrick SJ. Nutrition in orthopaedic surgery. J Bone Joint Surg [Am] I982;64:1263-72.
- 29. Tkatch L, Rapin CH, Rizzoli R, et al. Benefits of oral protein supplementation in elderly patients with fracture of the proximal femur. J Am Coll Nutr 1992;11:519-25.
- 30. Ammann P, Bourrin S, Bonjour JP, Meyer JM, Rizzoli R. Protein undernutritioninduced bone loss is associated with decreased IGF-I levels and estrogen deficiency. J Bone Miner Res 2000;15:683-90.
- 31. Smit E, Nieto FJ, Crespo CJ, Mitchell P. Estimates of animal and plant protein intake in US adults: results from the Third National Health and Nutrition Examination Survey, 1988-I991. JAm Diet Assoc I999;99:8I3-20.
- 32. Riggs BL, Melton LJ, 3rd. Evidence for two distinct syndromes of involutional osteoporosis. Am J Med 1983;75:899-901.
- 33. Heaney RP. Nutritional factors in osteoporosis. Annu Rev Nutr 1993; 13:287-316.

107

- 34. Fuller GF. Falls in the elderly. Am Fam Physician 2000;61 :2159-68, 2173-4.
- 35. Heaney RP. Pathophysiology of osteoporosis. Am J Med Sci 1996;312:251-6.
- 36. Riggs BL, Khosla S, Melton LJ, 3rd. A unitary model for involutional osteoporosis: estrogen deficiency causes both type I and type II osteoporosis in postmenopausal women and contributes to bone loss in aging men. J Bone Miner Res 1998;13:763-73.
- 37. Willett WC. Nutritional epidemiology. New York: Oxford Press, 1990.
- 38. Herzog AR, Rodgers WL. Age and response rates to interview sample surveys. J Gerontol 1988;43:S200-5.

CHAPTER 5

SUMMARY AND CONCLUSIONS

Summary

The general objectives of this dissertation project were first to evaluate a method of dietary assessment designed to estimate usual dietary intake in an elderly population for validity and reproducibility, and second to utilize that dietary assessment method in examination of a controversial diet-disease relationship of the aged. This dissertation consists of reports from two studies and one review paper. The first study describes the development of a picture-sort food frequency questionnaire (FFQ) designed specifically for an elderly population of Utah and reports correlations between mean nutrient intakes estimated by repeat administrations of the FFQ and between the FFQ and multiple 24 hour recalls, measuring reproducibility and validity of the method (Chapter 2). The review paper describes evidence surrounding the hypothesis that dietary protein intake is associated with bone health, osteoporosis, and risk of hip fracture in the elderly (Chapter 3). The second study applies the Utah picture-sort FFQ to elderly residents of Utah in a population-based case-control study designed to examine the relationship between total, animal, and vegetable protein intake and risk of hip fracture in the Utah population (Chapter 4).

Validation and Reproducibility of a Picture-Sort Food Frequency Questionnaire

The Utah picture-sort food frequency questionnaire (FFQ) was evaluated for validity and reproducibility of dietary assessment in a subgroup of controls from the

larger population-based case-control study in Utah. The picture-sort FFQ was designed specifically for the elderly population of Utah as an alternative to more traditional paperpencil FFQs in hopes that it would allow respondents with low literacy level, poor memory, or impaired vision and hearing, who may be otherwise excluded, to participate in the study.

The difference between validity and reproducibility of estimated usual dietary intake measured by the picture-sort FFQ for younger compared to older elderly participants (≤ 69 vs. > 69 years of age) was of special interest, and agreement between nutrient estimates made from the test and reference method were assessed by age and gender strata. Correlations between the first and second administration of the picture-sort FFQ, representing a measure of repeatability, were similar for younger and older men and women (range of mean correlations: 0.67- 0.69). Correlations between the first administration of the picture-sort FFQ and the average of multiple 24-hour recalls, representing a measure of validity, were similar for all men and younger women (range of mean correlations: 0.50- 0.55) but were slightly lower for older women (0.46). According to the literature, correlations between dietary assessment methods of above 0.30 are traditionally viewed as acceptable. Correlations less than 0.30 were observed in older men and women for vitamin A, and also in older women for protein and cholesterol. Results indicated that in general the picture-sort FFQ is a useful tool to measure usual dietary intake in the elderly although younger elderly $(\leq 69$ years of age) may report usual dietary intake slightly more accurately than older elderly (> 69 years of age). These differences, although small, may be important in studies of the elderly examining diet-disease relationships in those well over the age of 70 years.

Picture cards may allow better identification of foods and prompt memory in elders and thus improve accuracy of reported nutrient intakes. Cognitive and physical limitations associated with aging make gathering dietary data especially difficult in elderly populations, and as a result many respondents of advanced age are excluded from observational studies. Picture-sort FFQs may be a useful tool in gathering dietary data in populations that include participants of advanced age. Inclusion of the oldest old in population-based observational studies may yield additional information helpful in defining diet-disease relationships.

Protein and Risk of Hip Fracture in the Elderly: A Review

A large and growing body of evidence supports protein's role in bone health, but the association between dietary protein intake and osteoporotic hip fracture is less than clear. Protein is an important component of the bone matrix, and protein-containing supplements improve medical outcomes after hip fracture. Protein increases urinary calcium excretion, yet in the presence of adequate dietary calcium intake may not disrupt calcium balance or cause bone depletion. Results from observational studies are controversial. Most but not all report positive associations between protein intake and BMD, yet a few report increased hip fracture risk in groups consuming high protein diets.

Additional research is needed to clarify the relationship between dietary protein intake and risk of hip fracture in the elderly. Nutrient-nutrient, nutrient-gene, and nutrient-environment interactions may modify the relationship and will likely be important in future analyses. Other avenues for future research include examining the relationship by not only animal and vegetable protein sources but also by markers of

protein quality, such as specific amino acids, or by food groups. To date the evidence seems to support the view that higher dietary protein intake, obtained from a varied diet, and in the presence of adequate calcium and phosphorous intakes, seems more beneficial than harmful for bone health, especially to the elderly who are at increased risk for hip fracture.

Protein Intake and Risk of Osteoporotic Hip Fracture in Elderly Residents of Utah

A population-based case-control study of Utah residents aged 50 - 89 years was designed to examine the relationship between total, animal, and vegetable protein intake. Diet was assessed using the validated Utah picture-sort FFQ. Information about other risk factors for hip fracture was obtained in an in-person interview conducted at each participant's place of residence.

Differences in dietary protein intake between participants aged 50 - 69 years, 70 - 79 years, and 80- 89 years were observed, and younger participants (aged 50 - 69 years) consumed a larger percent of total calories from protein than did older participants (aged 70- 79 years or 80- 89 years). Logistic regression models were used to evaluate the relationships between the dietary protein variables and risk of hip fracture. After testing all combinations of interactions between protein intake, age, and gender, the interaction between protein intake and age was found to be highly significant and thus the results were stratified by age-group (50- 69 years olds, 70- 79 years olds, 80- 89 year olds). In logistic regression models that controlled for estrogen use, body mass index, smoking status, alcohol use, energy and calcium intake, physical activity, and the interactions between gender, age, and protein intake, the risk of hip fracture decreased across

increasing quartiles of total protein intake for participants aged 50- 69 years (OR: 1 (reference); 0.38 (95% CI: 0.21- 0.71); 0.59 (0.32- 1.10); 0.22 (0.11 - 0.45); p for trend $=$ < 0.001). No increase or decrease in risk across increasing quartiles of total protein intake were observed for participants aged 70 - 79 years or 80 - 89 years.

The effect of age-modification on the relationship between protein intake and risk of hip fracture is a unique feature to the analyses presented in this manuscript. Although other observational studies examining the relationship between dietary protein intake and risk of hip fracture have also observed similar dietary protein intake patterns, the effect of age-modification on the relationship has not been examined. This age-modification may in part explain the conflicting reports from previous studies.

Conclusions

The Utah picture-sort FFQ is a useful method of dietary assessment and can be used to estimate usual dietary intake in the aged. This method of dietary assessment may allow elders with cognitive and physical limitations associated with aging to participate in dietary studies. The Utah Study of Nutrition and Bone Health, a population-based case-control study, was designed to examine the relationship between dietary protein intake and risk of hip fracture in the elderly. Measurements of usual dietary intake needed to examine the diet-disease relationship in question were obtained using the Utah picture-sort FFQ. In the Utah population, higher total protein intake was associated with a reduced risk of hip fracture in men and women aged 50 - 69 years and did not appear to increase risk of hip fracture in men and women aged 70 - 89 years.

In the Utah study, the effect of dietary protein intake on risk of hip fracture appears to be modified by age. Including interactions between dietary protein intake and age in logistic regression models used to estimate risk of hip fracture across increasing quartiles of protein intake is a unique feature to the analyses. This interaction has not been controlled for in previous analyses of data from other observational studies. Identification of this age-modification in future research may help to clarify the relationship between dietary protein intake and risk of hip fracture.

Results from the analyses of this project, consistent with reports from several other studies, will help to promote the message that higher dietary protein intake appears more beneficial than harmful for bone health in the elderly. Dietary protein intake at or above current recommendations may be listed among other nutritional interventions useful in the prevention of osteoporotic fractures. Nutritional interventions such as modification of protein intake late in life may decrease the cost and burden associated with hip fracture and help many elders remain independent and have a higher quality of life in their later years.

APPENDICES

Appendix A. Demographic Characteristics

 \overline{a}

of Participants in the USNBH

Table A-1

Characteristics of men and women aged 50-89 years in the Utah Study of Nutrition and Bone Health.

Means \pm SD.

² Percent of total population

Appendix B. USNBH Interview Booklet

The Utah Hip Fracture Study Interview Questionnaire

NIH Grant Number R01-AR43391

Department of Nutrition and Food Sciences Utah State University Logan, UT 84322-4450

Revised 8-5-98

START TIME: U : W: AM or PM

 $\frac{1}{k}$

 \overline{r} and \overline{r}

 $\frac{1}{3}$

 $\overline{\overline{z}}$

READ THE FULL STATEMENT THEN HAND OVER THE "CLOSE YOUR EYES" PAPER. DO NOT REPEAT INSTRUCTIONS OR COACH. SCORE EACH PART BELOW.

 $\tilde{\mathbf{z}}$ $\frac{1}{2}$

 \checkmark

 $\ddot{}$

Now, I am going to ask you about individual vitamins, minerals, and other dietary supplements that you take by themselves. I would also like to know the strength or dose of the dietary supplement and how often you took them. You don't need to tell me again about the vitamins, minerals, and other dietary supplements we've already recorded.

$\ddot{\mathbf{v}}$

 $\bar{\epsilon}$

 $\bar{\mathbf{x}}$

!55

 $\bar{\lambda}$

 \mathbf{v}

N. FAMILY HISTORY OF BONE FRACTURE AND BONE DISEASE:

I would like to ask you about your blood relatives and whether or not any of them have ever had a hip fracture or other problems with their bones known as osteoporosis.

Osteoporosis includes broken bones due to bone loss and thinning of bones that occurs with aging, loss of height because of bone loss in the spine, or a "Dowager's hump" in the spine because of bone loss.

INTERVIEWER CHECK IF RESPONDENT IS FEMALE \rightarrow CONTINUE \cdots is \rightarrow **POINT:**

 $\ddot{\epsilon}$

Appendix C. The Utah Picture-Sort

FFQ Form

RESPONDENT ID: WWW.

175

Appendix D. Copyright Notice

Public Health Nutrition

Volume 4, 2001 ISSN: 1368-9800

Publishing, Production, Marketing, and Subscription Sales $O(f)$

CABI Publishing CAB International Wallingford Oxon OX10 8DE, UK

Tel: +44(0)1491 83211 $F_3x \t + 44(0)1491829292$ Email: publishing@cabi.org Telex: 847964 (COMAGG G)

For Customers In North America:

CABI Publishing 10 E 40th Street Suite 3203 New York, NY 10016

Tel: 212 481 7018 Toll-free: 800 528 4841 Fax: 212 686 7993 Email: cabi-nao@cabi.org CAB International also has regional offices in Malaysia, Trinidad & Tobago and Kenya

Publishing Director: David Nicholson

Special sales and supplements

This journal accepts advertising and inserts. We also provide bulk reprints of suitable papers to meet teaching or promotional requirements. The journal also publishes supplementary material including conference proceedings on behalf of academic and corporate sponsors. Please contact David Nicholson at the Wallingford address for further details.

Subscription information

Public Health Nutrition is an international journal published bimonthly by CABI Publishing (a division of CAB International) on behalf of the Nutrition Society

Annual subscription rates

Volume 4, 2001 (6 issues): £255.00

US Dollars (Americas and Japan only): \$455.00

Special rate for members of the Nutrition Society: £52.00 or \$85.00 (Americas only)

Japanese agent: Maruzen Company Ltd., PO Box 5050, Tokyo International, 100-31, Japan

Any supplements to this journal published in the course of the annual volume are normally supplied to subscribers at no extra charge

Claims for non-receipt of journal issues will be considered on their merit and only if the claim is received within six months of publication. Replacement copies supplied after this date will be chargeable.

Advertising: The Nutrition Society is willing to include advertisements in its journals. However, it will retain the right to make decisions on which advertisements are acceptable and which are not, and will not be obliged to give reasons to prospective advertisers for its decisions. The appearance of an advertisement in the Society's journals does not imply endorsement by the Society. For further details, please contact CABI Publishing at the Wallingford address.

Back volumes will be available in due course. Please contact CABI Publishing for further information.

Despatch: deliveries outside the UK are by ASP Printflow Airsaver unless other arrangements are made. Customers requiring airmail delivery should indicate clearly their requirements and add an additional 10% to the relevant subscription price

US POSTMASTERS: please send address corrections to CABI Publishing at the Wallingford address.

Notes for Authors are available from the publisher at the given address (Notes for Authors can be found inside the back cover).

Offprints: The author (or main author) of an accepted paper will receive 50 free offprints of their paper and a voucher copy of the issue in which their paper has been published. Additional offprints are available for a fee and should be ordered at proof stage. No page charges are levied by this journal.

Copyright: As of 1 January 2001 the copyright of all articles submitted to Public Health Nutrition are retained by the authors or their institutions. For articles prior to this date permission for reproduction of any part of the journal (text, figures, tables or other matter) in any form (on paper, microfiche or electronically) should be sought directly from the Society, at: The Editorial Office, The Nutrition Society, 10 Cambridge Court, 210 Shepherds Bush Road, Hammersmith, London, W6 7NI, UK.

Disclaimer: The information contained herein, including any expression of opinion and any projection or forecast, has been obtained from or is based upon sources believed by us to be reliable, but is not guaranteed as to accuracy or completeness. The information is supplied without obligation and on the understanding that any person who acts upon it or otherwise changes his/her position in reliance thereon does so entirely at his/her own risk. Neither the Society, nor CAB International accepts responsibility for any trade advertisement included in this publication

This journal is printed on acid-free paper from renewable sources. Typeset and printed by Alden Press, Oxford and Northampton, UK.

Public Health Nutrition is covered in CAB ABSTRACTS®, Index Medicus® (MEDLINE®). EMBASE/Excerpta Medica, BIOSIS® Database and CINAHL® Database

Appendix E. Release Letters from Coauthors

Nancy A. West Department of Nutrition and Food Sciences Utah State University Logan, Utah 84322

Dear Ms. West,

I am in the process of preparing my dissertation in the department of Nutrition and Food Sciences at Utah State University. I hope to complete my degree in the winter of 2001.

I am requesting your permission to include the article, *Comparison of a picture-sort food frequency questionnaire with 24-hour dietary recalls in an elderly Utah population,* of which I am first author, and you are a co-author, as a chapter in my dissertation. All coauthors of the manuscript will be acknowledged in a footnote to the chapter title in the dissertation.

Please indicate your approval of this request by signing in the space provided.

Sincerely

Heidi J. Wengreen

I hereby give permission to Heidi J. Wengreen to include the article, *Comparison of a picture-sort food frequency questionnaire with* ²⁴ hour *dietary recalls in an elderly Utah population,* in her dissertation. I understand all co-authors will be acknowledged in a footnote to the chapter title in the dissertation.

Signed M ancy West

Siew Sun Wong Department of Nutrition and Food Sciences Utah State University Logan, Utah 84322

Dear Ms. Wong,

I am in the process of preparing my dissertation in the department of Nutrition and Food Sciences at Utah State University. I hope to complete my degree in the winter of 2001.

I am requesting your permission to include the article, *Comparison of a picture-sort food frequency questionnaire with 24-hour dietary recalls in an elderly Utah population.* of which I am first author, and you are a co-author, as a chapter in my dissertation. All coauthors of the manuscript will be acknowledged in a footnote to the chapter title in the dissertation.

Please indicate your approval of this request by signing in the space provided.

Sincerely

Heidi J. Wengreen

I hereby give permission to Heidi J. Wengreen to include the article. Comparison of a $picture-sort$ food frequency questionnaire with 24-hour dietary recalls in an elderly U tah *population*, in her dissertation. I understand all co-authors will be acknowledged in a footnote to the chapter title in the dissertation.

Signed Siew San Wong

Nancy E. Sassano Department of Nutrition and Food Sciences Utah State University Logan, Utah 84322

Dear Dr. Sassano,

I am in the process of preparing my dissertation in the department of Nutrition and Food Sciences at Utah State University. I hope to complete my degree in the winter of 2001.

I am requesting your permission to include the article, *Dietary protein intake and risk of osteoporotic hip fracture in elderly residents of Utah,* of which I am first author, and you are a co-author, as a chapter in my dissertation. All co-authors of the manuscript will be acknowledged in a footnote to the chapter title in the dissertation.

Please indicate your approval of this request by signing in the space provided.

Sincerely

Heidi J. Wengreen

I hereby give permission to Heidi J. Wengreen to include the article, *Dietary protein* intake and risk of osteoporotic hip fracture in elderly residents of Utah, in her dissertation. I understand all co-authors will be acknowledged in a footnote to the chapter title in the dissertation.

Signed Namy Assam

Nancy A. West Department of Nutrition and Food Sciences Utah State University Logan, Utah 84322

Dear Ms. West,

I am in the process of preparing my dissertation in the department of Nutrition and Food Sciences at Utah State University. I hope to complete my degree in the winter of 2001.

I am requesting your permission to include the article, *Dietary protein intake and risk of osteoporotic hip fracture in elderly residents of Utah,* of which I am first author, and you are a co-author, as a chapter in my dissertation. All co-authors of the manuscript will be acknowledged in a footnote to the chapter title in the dissertation.

Please indicate your approval of this request by signing in the space provided.

Sincerely

Heidi J. Wengreen

I hereby give permission to Heidi J. Wengreen to include the article, *Dietary protein* intake and risk of osteoporotic hip fracture in elderly residents of Utah, in her dissertation. I understand all co-authors will be acknowledged in a footnote to the chapter title in the dissertation.

 $Signed$ $\frac{1}{\sqrt{2}}$ ancy $\frac{1}{\sqrt{2}}$ Date $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$

Jianjun Zhang Department of Nutrition and Food Sciences Utah State University Logan, Utah 84322

Dear Dr. Zhang,

I am in the process of preparing my dissertation in the department of Nutrition and Food Sciences at Utah State University. I hope to complete my degree in the winter of 2001.

I am requesting your permission to include the article, *Dietary protein intake and risk of osteoporotic hip fracture in elderly residents of Utah,* of which I am first author, and you are a co-author, as a chapter in my dissertation. All co-authors of the manuscript will be acknowledged in a footnote to the chapter title in the dissertation.

Please indicate your approval of this request by signing in the space provided.

Sincerely

Heidi J. Wengreen

I hereby give permission to Heidi J. Wengreen to include the article, *Dietary protein* intake and risk of osteoporotic hip fracture in elderly residents of Utah, in her dissertation. I understand all co-authors will be acknowledged in a footnote to the chapter title in the dissertation.

Signed Jlanjun 7/1ang Date $\frac{1}{\sqrt{2V_1 + 5} \cdot 2^{cC}}$

CURRICULUM VITAE

Heidi Jensen Wengreen (January 2002)

EDUCATION

PROFESSIONAL EXPERIENCE

PROFESSIONAL CREDENTIALS

 $10/97$ – present

Registered Dietitian, American Dietetics Association Member# 87102

PROFESSIONAL PRESENTATIONS

Wengreen HJ, Munger RG, West N, Cutler DR, Corcoran CD, Zhang J, Sassano NE. Protein Intake and Risk of Osteoporotic Hip Fracture in Elderly Utah Residents. International Conference on Nutrition and Aging, Paris, France, July 2001.

Wengreen HJ, Munger RG, West N, Cutler DR, Corcoran CD, Zhang J, Sassano NE. Protein Intake and Risk of Osteoporotic Hip Fracture in Elderly Utah Residents. Society for Epidemiologic Research Annual Meetings, Toronto, Canada, June 2001.

Wengreen, HJ, Munger, RG, West, N, Wong, SS. Comparison of a Picture-Sort Food Frequency Questionnaire to 24-hour Dietary Recalls in an Elderly Utah Population. Fourth International Conference on Dietary Assessment Methods. Tuscon, AZ. September 2000.

Wegreen, HJ, Munger, RG, West, N, Wong, SS. Comparison of a Picture-Sort Food Frequency Questionnaire to 24-hour Dietary Recalls in an Elderly Utah Population. Society for Epidemiologic Research Annual Meetings. Seattle, WT. June 2000.

Munger, RG, Wengreen, HJ, Wong, SS, West, N. Vitamin K Intake and Risk of Osteoporotic Hip Fracture in Utah Women. Society for Epidemiologic Research Annual Meetings. Seattle, WT. June 2000.

MacMahan, K, Wengreen, HJ, Schwaneveldt, N. Weight Loss in People Taking Phentermine-Fenfluramine With and Without Follow-up Consultations With a Registered Dietitian. American Dietetics Association Annual Meetings. Boston, MS. October 1997.

Christensen, N. Schroth, P, Allen, A, Wengreen, H, Spencer, S, et al. Potassium content of foods after cooking and acceptability of taste in people on dialysis. Utah Dietetics Association Annual Meetings. Park City, UT. April 1997.

PUBLICATIONS

Wengreen, HJ, Munger, RG, West N, Wong, SS. Comparison of a Picture-Sort Food Frequency Questionnaire to 24-hour Dietary Recalls in an Elderly Utah Population. PHN 200 I ;4 :961-970.

189