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Bone Mineral Density and Protein-Derived Food Clusters from the Framingham Offspring Study

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ABSTRACT

Background Dietary protein is beneficial to bone health; however, dietary patterns of protein intake and their relationship with bone mineral density (BMD) have not been evaluated.

Objective To examine the relationship of dietary protein food clusters with BMD at the femoral neck, trochanter, total femur, and lumbar spine among middle-aged and older men and women.

Design Cross-sectional study.

Participants and setting Two thousand seven hundred fifty-eight community-dwelling individuals from the Framingham Offspring Study.

Methods BMD was measured by Lunar DPX-L (Lunar Radiation Corporation) in 1996-2001. Dietary intakes were estimated using the Willett food frequency questionnaire in either 1995-1998 or 1998-2001, and the exam closest to a participant's BMD measurement was used. Cluster analysis (FASTCLUS procedure, k-means method) was used to classify participants into groups, determined by major sources of protein. Generalized linear regression was used to compare adjusted least-squares mean BMD across protein food clusters for all pairwise comparisons.

Results From 2,758 participants (44% men; mean age 61±9 years, range=29 to 86 years), five protein food clusters were identified (chicken, fish, processed foods, red meat, and low-fat milk). Three of these food clusters showed associations with BMD. The red meat protein food cluster presented with significantly lower femoral neck BMD compared with the low-fat milk cluster (red meat 0.898±0.005 g/cm^2 vs low-fat milk 0.919±0.007 g/cm^2; P=0.04). Further, the processed foods protein cluster presented with significantly lower femoral neck BMD compared with the low-fat milk cluster (processed foods 0.897±0.004 g/cm^2 vs low-fat milk 0.919±0.007 g/cm^2; P=0.02). A similar, yet nonsignificant, trend was observed for other BMD sites examined.

Conclusions Diets with the greatest proportion of protein intake from red meat and processed foods may not be as beneficial to the skeleton compared with dietary patterns where the highest proportion of protein is derived from low-fat milk.
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OSTEOPOROSIS AND LOW BONE MASS CURRENTLY affect approximately 44 million US adults older than age 50 years.[1] Worldwide, one in three women in this age group will experience osteoporotic-related fractures, as will one in five men.[2-4] The debilitating health consequences of osteoporotic fracture include chronic pain, reduced mobility, disability, and increasing degree of dependence. Perhaps most strikingly, mortality rates increase 20% to 24% within the first year after experiencing a hip fracture.[5] Therefore, it is of utmost public health importance to prevent this widespread disease.

Modifiable lifestyle interventions, such as altering dietary intake, have the potential to prevent or forestall bone loss associated with aging. Studies suggest that dietary protein is protective of bone loss over time[6] and may benefit the skeleton by increasing insulin-like growth factor-1,[7] augmenting intestinal calcium absorption,[8,9] and improving muscle strength and mass.[10,11] However, in most epidemiologic studies, protein intake is examined as a single macronutrient with little consideration of its food source and consumption with other foods in the diet. Protein-rich foods differ not only in their protein content, but also in their amino acid composition, digestibility, and synergy with other nutrients.[12] Dietary protein may interact with nutrients found in non–protein-rich foods consumed simultaneously in a meal.[13] Previous research by our group has shown

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different dietary patterns (derived from energy intake) to be associated with bone health.[14] Therefore, it is crucial to expand this dietary pattern methodology by examining patterns of protein intake to understand the complex relationship of dietary protein (usual intake, as consumed with other foods and nutrients) with bone health in independent-living adults.

The purpose of this cross-sectional study was to examine the association of dietary protein food clusters (derived from novel dietary pattern techniques) with bone mineral density (BMD) at the hip and spine among middle-aged and older Framingham Offspring Study participants. In contrast to previous studies with a priori hypotheses that specific protein-rich foods may be more beneficial to bone health, we chose to examine the diets of community dwelling middle-aged and older adults, utilizing novel protein-centric food patterning techniques. Although our use of protein as the primary nutrient in cluster analysis is novel (typically total energy intake is used), the dietary patterning methodology in this study has been previously validated in the Framingham Cohorts.[15] We hypothesized that multiple protein food clusters could be created using this systematic method of grouping, and that not all protein food clusters would be equally beneficial to bone health.

METHODS

Subjects

The Framingham Offspring Study is a longitudinal cohort study that began in 1971 by enrolling 5,124 adult children of the Original Framingham Study and their spouses.[16] The purpose of the Framingham Study was to identify risk factors for coronary artery disease, including familial factors. Visits occur every 4 to 8 years, where participants take part in physical examinations, blood chemistries, assessment of risk factors, and questionnaires. Of the 5,124 Offspring Study participants, 2,764 men and women completed a validated food frequency questionnaire (FFQ) either in 1995-1998 or 1998-2001. We excluded participants with missing/incomplete FFQ, based on the criteria of more than 12 food items left blank or with energy intakes $<$600 kcal/day or $>$4,000 kcal/day. Of the 2,764 men and women, six participants were removed following outlier analyses (as explained in the statistical analysis section). Two thousand seven hundred fifty-eight participants were included in the cluster analysis to create protein dietary patterns (described thoroughly in the statistics section based on previously used[17,18] and validated techniques[15]). Participants with missing covariate information on age, height, body mass index (BMI), smoking status, calcium and vitamin D supplement use, or estrogen status were excluded after performing cluster analysis (n=17). Hence, 2,741 participants were used to describe the sample. In this cohort, BMD measures were performed between the years 1996-1998 or 1998-2001. Dietary information collected closest to participants' BMD measurement date was used in subsequent analyses (mean time difference between FFQ and BMD measurements was 255±235 days). The final analytic sample included 2,721 Framingham Offspring Cohort study participants with protein cluster and BMD data. All participants provided informed consent for their participation. This study was approved by the Institutional Review Board at Hebrew SeniorLife.

BMD

BMD was measured at the hip (regions of interest were femoral neck, trochanter, and total femur) and lumbar spine (average BMD of L2 to L4) in grams per centimeter^2 using dual energy x-ray absorptiometry (Lunar DPX-L; Lunar Radiation Corporation). The right hip was scanned unless there was a history of previous fracture or hip joint replacement, in which case the left hip was scanned. The precision was 1.7% at the femoral neck, 2.5% at the trochanter, and 0.9% at the spine, which is similar to the range of 1.8% to 1.9% reported by others.[19,20]

Dietary Assessment

Usual dietary intakes of foods and nutrients were assessed with a semiquantitative and validated 126-item FFQ.[21,22] Questionnaires were mailed to participants before each examination, and the participants were asked to complete them and bring them to the exam. This FFQ has been validated for many foods and nutrients and against multiple diet records or blood measures in several populations.[21,23-25] Total daily protein contribution in grams per day from each food consumed was calculated from the food list section of the FFQ. Percent protein contribution from individual foods to total protein intake was calculated for all participants using the equation [(protein from specific food (g) divided by total protein intake (g))$\times$100] for use in cluster analysis.

Covariates

Covariates known to affect bone health were included in all statistical analyses. Covariates were captured at the exam when diet was measured (either 1995-1998 or 1998-2001). These covariates included age (in years), sex, menopause status, and use of estrogen (women only), height (in meters), BMI, physical activity (continuous score), total energy intake (in kilocalories per day), smoking status (never, former, or current), alcohol intake (in grams per day), calcium supplement use, and vitamin D supplement use. Height was measured without shoes to the nearest 0.25 in (0.64 cm) with the use of a stadiometer. Weight was measured in pounds with the use of a standard balance-beam scale (Detecto, Worcester Scale Co, Inc). These measures were converted to meters and kilograms, respectively, and BMI was then calculated as weight in kilograms/height in meters^2. Physical activity level was assessed using the Physical Activity Scale for the Elderly, a validated questionnaire of self-reported activity over the past 7 days.[26]

Usual intakes of total energy and alcohol were assessed with the FFQ. Smoking status was defined as never, former, or current smoker. Women were classified as estrogenic (premenopausal or currently taking postmenopausal estrogen) or nonestrogenic (postmenopausal and non–estrogen user) based on the following self-reported variables: current estrogen use (yes or no) and menopausal status (menstrual periods stopped for 1 year [yes or no]).

Supplement use was captured in the supplement section of the FFQ. Calcium supplement use was then categorized as non–supplement user (0 mg/day); supplement use from a multivitamin (supplemental calcium intake $>$0 and $<$200 mg/day); or additional supplement use (supplemental calcium $\geq$200 mg/day). Vitamin D supplement use was categorized similarly: non–supplement user, supplement use