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Dietary acid load is associated with lower bone mineral density in men with low intake of dietary calcium

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Abstract

High dietary acid load (DAL) may be detrimental to bone mineral density (BMD). The objectives of the study were to: 1) evaluate the cross-sectional relation between DAL and BMD; 2) determine whether calcium intake modifies this association. Men (n=1218) and women (n=907) 60y were included from the National Health and Nutrition Examination Survey 2005–2008. Nutrient intake from 2–24h recalls was used to calculate net endogenous acid production (NEAP) and potential renal acid load (PRAL) (mEq/d). PRAL was calculated from dietary calcium (PRAL_{diet}) and diet + supplemental calcium (PRAL_{total}). Tests for linear trend in adjusted mean BMD of the hip and lumbar spine were performed across energy adjusted NEAP and PRAL quartiles. Modification by calcium intake (dietary or total) above or below 800 mg/d was assessed by interaction terms. Overall, mean age was 69 ± 0.3y. Among women, there was no association between NEAP and BMD. PRAL_{diet} was positively associated with proximal femur BMD (p trend=0.04). No associations were observed with PRAL_{total} at any BMD site (P-range: 0.38–0.82). Among men, no significant associations were observed of BMD with NEAP or PRAL. However, an interaction between PRAL_{diet} and calcium intake was observed with proximal femur BMD (p=0.08). An inverse association between PRAL_{diet} and proximal femur BMD was detected among men <800 mg/d dietary calcium (p=0.02); and no associations ≥ 800 mg/d (p=0.98). A significant interaction with PRAL_{total} was not observed. In conclusion, when supplemental calcium is considered, there is no association between DAL and BMD among adults. Men with low dietary calcium showed an inverse relation with PRAL at the proximal femur; in women no interaction was observed. This study highlights the importance of calcium intakes in counteracting the adverse effect of DAL on bone health. Further research should determine the relation between DAL and change in BMD with very low calcium intake.

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Keywords

dietary acid load; BMD; NHANES; calcium intake; dietary protein

Introduction

Osteoporosis is characterized by low bone mass and can lead to increased risk of fracture at the hip, spine, and wrist (1, 2). Hip fractures have debilitating consequences, with mortality rates up to 24% one year post-fracture (3) and are a major economic burden (4, 5). Due to the inherent loss in quality of life and large medical costs following an osteoporotic fracture, prevention of this disease is a public health priority. The acid generating capacity of the western diet (because of its high animal protein content) has been implicated as a potential contributor to bone loss. This hypothesis, however, remains controversial.

Dietary protein is a primary contributor to dietary acid load (DAL), mainly through the metabolism of methionine and cysteine to sulfuric acid (6). Concurrently, plant foods also generate base-forming constituents, primarily in the form of bicarbonate (7). The calculation of DAL from dietary constituents is termed net endogenous acid production (NEAP) and it includes both the acid and the base generating capacity of the entire diet. Data from the third National Health and Nutrition Examination Survey (NHANES) show the average American diet to be acid producing, with an NEAP of positive 48 mEq/d (8). Chronic disruption in the extracellular pH, such as with higher NEAP, may activate compensatory mechanisms to return the acid-base disruption to equilibrium (7).

In theory, the skeleton could act as a primary buffer system, where calcium is released from the bone matrix to counteract the acidic environment generated by higher NEAP. Previous research suggested that chronic acidosis results in augmented osteoclastic bone resorption and decreased osteoblastic bone formation (9). The result of the increased bone resorption was a concurrent increase in urinary calcium (10–12). However, recent research suggests that greater dietary calcium intake may offset the calciuric effect of protein on the bone matrix (13). Therefore, greater NEAP may only be detrimental to bone under conditions of low calcium intake. Therefore, the ability of calcium to modify the association between NEAP and bone health warrants further investigation.

The current epidemiological literature examining the potential association between DAL and bone are conflicting (14–18) and those measuring long term fracture risk have shown null results (19). However, randomized control trials using change in bone mineral density (BMD) as an outcome measure in postmenopausal women have shown that bone loss can be reversed with the addition of a base (either potassium citrate and/or calcium citrate) (20–23). It has yet to be determined whether chronic ingestion of an acid generating diet can be of sufficient magnitude to induce significant bone loss over time.

The current study aims to determine the cross-sectional association of DAL with BMD of the hip and spine among older men and women from recently available NHANES data. We hypothesized that higher DAL, estimated by NEAP, would be negatively associated with BMD in those participants with low calcium intake.

Methods

Sample Population and Data Collection

NHANES is the only national survey that collects extensive health information from both face-to-face interviews and medical examinations. It is designed to provide a cross-sectional

picture of health and nutrition in the U.S. population. The survey uses a complex, stratified, multistage, probability-cluster sampling design. A detailed description of the NHANES plans and procedures has been provided elsewhere (24).

The National Center for Health Statistics (NCHS) collects NHANES data in biennial cycles. The analyses reported in this paper utilized data from the 2005–2006 and 2007–2008 cycle. Men and women aged 60 y and older were included in the study sample because they are at greatest risk for osteoporosis and fracture. In total, 1,218 men and 907 women were included in the current analysis. Due to the amount of missing lumbar spine BMD data among women, survey analysis could not be conducted in this sub-group. Individuals with osteoporosis or those taking osteoporosis related medications were not excluded from analyses. Written informed consent was obtained from all participants or proxies, and the survey protocol was approved by the Research Ethics Review Board of NCHS (25).

Dietary Interview and Analysis

The objective of the dietary interview component is for the subject to recall all types and amounts of food consumed in a 24-h period of time. The dietary interview was conducted in person at a mobile examination center. All interviewers completed an intensive one week training course and were monitored during the interview process. Data were collected by NHANES interviewers using a US Department of Agriculture (USDA) dietary data collection instrument, the Automated Multiple Pass Method (26). This method uses a five-step procedure to quantify 24-h food intake (27, 28). The USDA's Food and Nutrient Database for Dietary Studies, Version 3.0 was used with the 2005–2006 data, and Version 4.1 was used for the 2007–2008 data. In the present study, only data on survey participants with dietary recall status codes of “reliable” were used. A code of reliable indicates that there were no missing reference values for any nutrient based on food items cited in the 24-h recall. Nutrient intake was calculated by averaging the two days of recall.

The NHANES 2005–2008 oversampled low-income persons, adolescents 12–19 years, persons 60+ years of age, African Americans, and Mexican Americans. To account for this, sampling weights are provided to support estimation of unbiased summary statistics for the US population. Sampling weights specifically related to the sub-sample of survey participants who completed the 24-h dietary recall were used in all analyses.

BMD Measurements

BMD (g/cm^2) of the spine and hip was measured by dual-energy X-ray absorptiometry on all eligible participants. Only individuals designated in NHANES with valid BMD scans were used in statistical analyses. Invalidity codes were provided to indicate the reasons which some scans could not be analyzed accurately (such as excessive x-ray noise due to obesity, jewelry or other objects not removed, non-removable objects, movement or positioning problems, degenerative diseases, spinal fusion or fractures). Both the femur and spine scans were performed with a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc., Bedford, Massachusetts) using Hologic software version 8.26:a3* through mid 2005 and Hologic Discovery software (v12.4) thereafter (for femur scans) and Hologic APEX v3.0 software (for the lumbar spine). The left hip was routinely scanned. In the case of left hip fracture, pin, or replacement, the right hip was scanned. Rigorous quality control standards were routinely employed and further detail can be found elsewhere (29).

Covariates

Covariates thought to affect bone health were included in all statistical analyses. Such demographic covariates included: age (y) and ethnicity (White non-Hispanic, Black non-Hispanic, Mexican American, Hispanic/Other). General health was assessed by height (cm),

weight (kg), physical activity (created by combining existing variables in NHANES to assess leisure activity by none, moderate and vigorous), or use of hormone replacement therapy among women only. Lifestyle factors included alcohol consumption (4 levels) cigarette smoking (4 levels) and caffeine intake (mg/d). Prescription medication use of thiazides and/or bisphosphonates were captured as dichotomous variables (use yes/no). Nutrients included in analyses were total energy intake (kcal/d), dietary magnesium (mg/d), dietary calcium (mg/d) and total calcium intake from diet and supplements combined (mg/d). Dietary vitamin D data are not available for NHANES years 2005–2006; therefore dietary vitamin D was not included in these analyses. Nutrition supplement use over the past 30d was captured during the in-person interview. Supplemental vitamin D use was assessed as a dichotomous variable (use: yes/no). Supplements included single- and multi-ingredient non-prescription vitamin or mineral supplements, antacids, and prescription supplements. Calcium supplementation was assessed as a dichotomous variable (use: yes/no) for adjustment in NEAP models. Further, calcium supplementation was assessed in mg/d as it was included in the calculation of $PRAL_{total}$.

Dietary acid load

Dietary acid load was estimated by NEAP, which results predominantly from the amount of net acid (acid minus base) produced by the metabolic system every day (7). Estimated NEAP was calculated from two commonly used algorithms (30). The first calculation by Frassetto et al. estimates DAL from dietary protein (an acid precursor) and potassium (an index of base precursors from organic anions) and has been previously validated in healthy men and women (age range: 17–73y) (31):

$$\text{Estimated NEAP (mEq/d)} = [0.91 \times \text{protein (g/d)}] - [0.57 \times \text{potassium (mEq/d)}] + 21.$$

This equation involves only the protein: potassium ratio and does not include other pH-altering nutrients from the diet, which are also believed to influence bone. Therefore, the following algorithm developed by Remer et al. (32) was used to calculate DAL. This equation estimates the potential renal acid load (PRAL) from average intestinal absorption rates of ingested protein and additional minerals:

$$PRAL \text{ (mEq/d)} = 0.49 \times \text{protein (g/d)} + 0.037 \times \text{phosphorus (mg/d)} - 0.021 \times \text{potassium (mg/d)} - 0.026 \times \text{magnesium (mg/d)} - 0.013 \times \text{calcium (mg/d)}.$$

This method of calculation was experimentally validated in healthy adults (12) and children (33) under controlled conditions. PRAL was calculated in two ways: first from dietary calcium alone ($PRAL_{diet}$) and then from dietary and supplemental calcium intakes combined ($PRAL_{total}$).

Statistical analyses

Descriptive statistics were calculated for men and women separately by mean and standard errors and percentages for categorical variables using survey methodology. Prior to multivariate analyses, all variables were tested for normality and transformed by logarithmic or root transformation as appropriate. In previous work by Mclean and colleagues (15) the relation between DAL and BMD was observed in men, but not in women. Therefore, all analyses in the present study were stratified by sex.

Estimated NEAP and PRAL were adjusted for total energy intake using the residual method (34) and energy adjusted sex-specific quartiles of NEAP and PRAL were created. To

evaluate the relation between estimated NEAP, PRAL and BMD, analysis of covariance was used to test for a linear trend in the least squares-adjusted mean BMD at the femoral neck, proximal femur and lumbar spine (in men only) across estimated NEAP and PRAL quartiles. In this study, data pertaining to lumbar spine BMD were not examined in women because some of the primary sampling units in the NHANES survey included zero women with DXA data at the spine. This circumstance precluded the application of statistical techniques for survey data analysis. Estimates of BMD were transformed from the logarithmic or square root scale. The delta method was used to transform standard errors for means on the logarithmic and square root scale (35). Models were adjusted for age, height, weight, total energy intake, physical activity, smoking, alcohol intake, caffeine, vitamin D supplement use, calcium supplement use, dietary calcium, dietary magnesium and use of hormone replacement therapy (in women only). Because PRAL is calculated in part from calcium and magnesium intake, these variables (dietary calcium, dietary magnesium and supplemental calcium) were excluded from all PRAL multivariate models to avoid collinearity. To assess whether calcium intake plays a moderating role between DAL and BMD, interactions were tested with NEAP and PRAL as continuous ordinal variables and calcium intake categorized by <800mg/d or ≥800mg/d (calculated from dietary calcium alone, then again from total calcium intake including supplemental intake). Calcium was stratified by 800mg/d based on previous literature (15) and the distribution of the current data. Significance was set at $p < 0.05$. When testing interaction terms, significance was set at $p < 0.10$. All analyses were performed using SPSS software version 18 and StataIC software version 10.

Results

Subject characteristics can be found in Table 1. The database included 1,218 men and 907 women; mean age was 69 y. Mean energy intake per day was 2035 ± 39 kcal for men and 1577 ± 22 kcal for women; mean protein intake 82 ± 2 g/d and 62 ± 1 g/d for men and women respectively; mean dietary calcium was 910 ± 24 mg/d among men and 777 ± 19 mg/d among women. Mean NEAP and PRAL estimates are consistent with previous research (15, 17) (NEAP: 52.2 ± 0.7 , 48.0 ± 0.8 mEq/d; PRAL_{diet}: 8.5 ± 0.8 , 2.8 ± 0.6 mEq/d for men and women respectively). Men with total calcium intakes <800 mg/d had an average dietary calcium intake of 542 ± 13 mg/d, compared to an average dietary intake of 1095 ± 28 mg/d in men with intakes ≥800 mg/d. Women with total calcium intakes <800 mg/d had an average dietary calcium intake of 504 ± 11 mg/d, and those with total calcium intakes ≥800 mg/d had an average dietary calcium intake of 931 ± 21 mg/d.

Among women, no significant interactions were observed between calcium intake (above or below 800mg/d) and NEAP, PRAL_{diet} or PRAL_{total} in the models assessing hip BMD (P -range: 0.22–0.98). In the full model, no statistically significant association was observed between estimated NEAP and BMD at either the proximal femur or femoral neck (P -range: 0.10–0.16, Table 2). PRAL_{diet} was not significantly associated with femoral neck BMD ($P=0.16$, Table 3); however it was significantly associated with greater proximal femur BMD at quartiles 3 and 4 compared to quartile 2 ($P=0.045$). When total calcium intake (diet + supplements) was used to calculate PRAL_{total}, no significant associations were observed between PRAL_{total} at any BMD site (P -range: 0.38–0.82).

In men, significant interaction was observed between quartiles of PRAL_{diet} and dietary calcium intake (above or below 800mg/d) for proximal femur BMD ($P=0.08$) but not for other bone sites examined (P -range: 0.31–0.34). However, no significant interactions were observed between total calcium intake (above or below 800mg/d) and quartiles of PRAL_{total} (P -range: 0.26–0.86) or NEAP (P -range: 0.34–0.93) at any BMD site.

Among men, full models showed no statistically significant association between estimated NEAP and BMD at the proximal femur, femoral neck or lumbar spine (P -range: 0.46–0.83, Table 2). Further, no statistically significant association was observed between quartiles of $\text{PRAL}_{\text{diet}}$ (P -range: 0.34–0.57, Table 3) or quartiles of $\text{PRAL}_{\text{total}}$ (P -range: 0.22–0.73) and BMD at the hip or spine. Multivariable analyses for $\text{PRAL}_{\text{diet}}$, stratified by high and low calcium intakes, showed a significant inverse association between quartiles of $\text{PRAL}_{\text{diet}}$ and BMD at the proximal femur among men with <800 mg/d dietary calcium intake ($p=0.02$). While no associations were observed among men with calcium intake ≥ 800 mg/d ($p=0.98$).

In men and women, models assessing the relation between NEAP and BMD as well as PRAL and BMD did not change with the addition of additional covariates known to affect bicarbonate excretion (prescription thiazide use) or BMD (prescription bisphosphonate use) (data not shown).

Discussion

Overall, our results do not support the hypothesis that DAL is detrimental to bone health under conditions of normal calcium intake. Despite a modest association between quartiles of PRAL and proximal femur BMD among women, this association was not consistent at any other BMD site in women or men and was attenuated when calcium supplementation was included in the PRAL estimation. Further, estimated NEAP was not associated with BMD at any site in this cohort of older adults. Evidence of a significant interaction between dietary calcium and $\text{PRAL}_{\text{diet}}$ in relation to proximal femur BMD was observed in men, where lower BMD was associated with greater $\text{PRAL}_{\text{diet}}$ among those with dietary calcium intakes <800 mg/d. This interaction was not observed in women.

Our general negative finding of no association between DAL and BMD among men and women are in line with other recently published manuscripts. Data from the European Prospective Investigation into Cancer cohort found no significant association between PRAL and BMD as measured by tibial peripheral quantitative computed tomography among women over 60 y of age (16). Wynn and colleagues (18) reported a relatively weak inverse association between NEAP and broadband ultrasound attenuation (heel ultrasound) only among older women with a history of fracture. Results from the Framingham Osteoporosis Study reported no significant relation between estimated NEAP and PRAL with BMD at any site among women (15). Among men ≥ 70 y of age, estimated NEAP, but not PRAL, was inversely associated with femoral neck BMD. However, this association was not statistically significant at any other BMD site among this cohort of older men (mean age 76y, range: 68–92y), and was not observed at any site in men <70y (mean age 60y, range: 35–86y). Results from the current study found no association between estimated NEAP or PRAL with BMD at any site among men with an average age of 69y. However, among men with low dietary calcium intakes, an inverse relationship was observed with $\text{PRAL}_{\text{diet}}$ at the proximal femur. Interestingly, this association was not observed with total calcium intake, suggesting this interaction may only occur at very low calcium intake.

Higher calcium intake may influence the net effect of protein on the skeleton by resulting in greater calcium absorption and by lowering overall bone turnover rates (13). In a randomized clinically controlled trial in men and women >65y, calcium citrate malate supplementation plus vitamin D or placebo was provided for 3y and resulted in reduced bone loss from the spine, hip and total body (36). Further, increased protein intake was associated with a favorable change in total body BMD in the supplemented group, but not in the placebo group. This study suggests that protein may be favorable to bone under conditions of higher calcium intake, where there was an observed additional 25 mEq of alkali potential. Our results show a negative association between the acid production of the

diet, estimated by quartiles of PRAL, and BMD at the proximal femur among men with dietary calcium intakes <800mg/d. Further, this interaction was no longer significant when calcium supplementation was included in analyses, indicating that the interaction may only occur at relatively low intakes of calcium. In contrast, MacDonald et al. (37) found no effect of potassium citrate or increased fruit and vegetable consumption on BMD over time. A recent meta-analysis by Fenton et al. (38) concluded that the potential association between dietary acid load and osteoporotic bone disease is not supported by evidence. It appears doubtful that a diet high in acid-forming nutrients produces such a severe state of acidosis as to overwhelm the body's first several line of buffering mechanisms (intra and extra cellular buffers, pulmonary, and renal) to the point that calcium is mobilization from bone (39, 40).

Protein may have anabolic effects on bone turnover by increasing levels of IGF-1, promoting calcium absorption, suppressing parathyroid hormone, and improving muscle strength and mass (41). On the other hand, protein is a major contributor to DAL through the metabolism of its amino acids to sulfuric acid, which may be detrimental to bone. A harmonizing theory combining the two conflicting hypotheses was proposed by Thorpe and colleagues (17). In cross-sectional analyses, protein alone did not predict lumbar spine BMD among postmenopausal women. However, after controlling for the sulfate content of the diet, protein intake was a positive predictor of lumbar spine BMD. When considering other components of the diet, estimated PRAL was not a significant predictor of BMD at the hip or spine. The authors concluded that the positive association observed between protein intake and BMD is suppressed by a negative association of sulfur from amino acids at the lumbar spine. The negative effects of sulfur amino acids on bone may offset the beneficial effects of protein in the current study, resulting in the null response observed between estimated NEAP and PRAL with BMD.

Our study has inherent strengths and limitations. The data from NHANES are collected from diverse sub-populations and therefore, the results are generalizable to both men and women of multiple ethnic groups. Due to the cross-sectional nature of the current study it is unclear whether estimated NEAP or PRAL may influence change in BMD over time and causality cannot be assessed. Dietary intake was assessed by two, 24-h recall assessments and averaged over the two days to eliminate within person variation. However, this methodology does not correct for systematic bias that can create excess noise in the estimation of dietary intake. Methods assessing usual intake of nutrients by accounting for such variation are available (42, 43); however, use of these methods in multivariate analyses is currently under development. Further, there is evidence of an inverse association between urine ammonia and BMD among calcium kidney stone formers with hypercalciuria (44). However, because NHANES did not capture kidney stone formation in the 2005–2006 cycles we were unable to control for this potential confounding variable.

In conclusion, when supplemental calcium intake is considered, the results from this study do not support the overall hypotheses that DAL is associated with lower BMD among older adults. Among men with lower dietary calcium intakes, greater estimated PRAL was associated with significantly lower proximal femur BMD; however, these results were attenuated with the addition of calcium intake from supplements. This study highlights the importance of calcium intakes in counteracting the adverse effect of dietary acid load on bone health. Prospective studies are needed to determine the potential relationship between DAL and change in BMD at very low levels of calcium intake.

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The authors' responsibilities were as follows: KMM, SJW and JEK were responsible for the conception and design of the study as well as study execution; KMM, and SJW, for the acquisition of data, data management and statistical analysis. All authors were involved in the interpretation of data, and critically revising the manuscript for important intellectual content (KMM, SJW, JEK, AMK and KLI).

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Table 1

Descriptive statistics for men and women with valid 2-day 24h recalls and bone mineral density, data from the NHANES years 2005–2008^{1,2}

	Men	Women
n	1218	907
Age, y	69.4 ± 0.3	69.5 ± 0.3
Ethnicity (%)		
Mexican American	4.2 ± 0.8	4.6 ± 0.7
Hispanic, Other	5.9 ± 1.4	5.6 ± 0.1
White (non-Hispanic)	82.4 ± 2.4	80.1 ± 0.2
Black (non-Hispanic)	7.5 ± 1.2	9.7 ± 0.1
Height, cm	174.0 ± 0.2	160.9 ± 0.3
Weight, kg	86.1 ± 0.6	72.4 ± 0.7
% HRT ³ use	--	7.6 ± 1.4
Physical activity (%)		
None	42.6 ± 2.5	9.9 ± 1.3
Moderate	37.7 ± 1.8	36.4 ± 1.9
Vigorous	19.7 ± 2.4	53.7 ± 2.3
Smoking status (%)		
Never	32.1 ± 1.9	56.3 ± 2.1
Former	55.0 ± 2.3	29.8 ± 2.1
Current, 1 pack per day	9.8 ± 1.3	11.9 ± 1.4
Current, > 1 pack per day	3.1 ± 0.9	2.0 ± 0.8
Alcohol consumption (%)		
< 1 drink/mo	53.1 ± 2.8	68.3 ± 2.6
1 drink/mo & < 1 drink/wk	8.6 ± 1.2	9.2 ± 1.3
1 drink/wk & < 1 drink/d	29.0 ± 2.4	17.2 ± 1.9
1 drink per day	9.3 ± 1.1	5.4 ± 1.3
Nutrient Intakes (per day)		
Energy (kcal)	2035 ± 39	1577 ± 22
Protein (g)	82 ± 2	62 ± 1
Dietary Calcium (mg)	910 ± 24	777 ± 19
(% <800mg)	46 ± 2	59 ± 2
Total Calcium (mg)	1095 ± 35	1168 ± 44
Potassium (mg)	2923 ± 62	2388 ± 44
Phosphorous (mg)	1339 ± 31	1054 ± 22
Magnesium (mg)	304 ± 7	253 ± 5
Caffeine (mg)	180 ± 7	150 ± 8
Sodium (mg)	3372 ± 84	2603 ± 46
Supplement user (%)		
Vitamin D	47.0 ± 2.9	56.8 ± 2.2
Calcium	55.7 ± 2.5	65.9 ± 2.2

	Men	Women
Dietary acid load, mEq/d		
Estimated NEAP ⁴	52.2 ± 0.7	48.0 ± 0.8
PRAL _{diet} ⁵	8.5 ± 0.8	2.8 ± 0.6
PRAL _{total} ⁶	6.1 ± 0.82	-2.3 ± 0.68
Bone mineral density, g/cm ² *		
Proximal femur	0.988 ± 0.005	0.846 ± 0.006
Femoral neck	0.797 ± 0.005	0.721 ± 0.005
Lumbar spine	1.087 ± 0.009	---
T-score ⁷		
Proximal femur	-0.418 ± 0.040	-0.901 ± 0.048
Femoral neck	-0.785 ± 0.041	-1.100 ± 0.045
Lumbar spine	0.338 ± 0.069	---

¹ NHANES = The National Health and Nutrition Examination Survey

² Values are means ± SE

³ HRT= hormone replacement therapy (among women only)

⁴ NEAP = estimated net endogenous acid production

⁵ PRAL_{diet} = potential renal acid load (calculated from dietary calcium)

⁶ PRAL_{total} = potential renal acid load (calculated from dietary + supplemental calcium)

⁷ T-score = (Actual BMD – reference BMD)/SD of reference BMD. Reference group BMD: age 30–39y from the Center for Disease Control and Prevention, “Lumbar Spine and Proximal Femur Bone Mineral Density, Bone Mineral Content, and Bone Area: United States, 2005–2008”. Published 2012. (45)

* Bone mineral density adjusted for age.

Least square adjusted means and standard errors for BMD at proximal femur, femoral neck and lumbar spine by quartiles of estimated NEAP, data from the NHANES years 2005–2008^{1–5}

Table 2

	NEAP Quartile				p-trend
	1	2	3	4	
MEN					
n	282	286	285	365	
Dietary protein (g)	66 ± 2	83 ± 3	87 ± 2	91 ± 5	
Dietary calcium (mg)	913 ± 39	1018 ± 49	915 ± 33	795 ± 36	
Estimated NEAP range	6.87 – 38.82	38.86 – 49.40	49.41 – 62.50	62.53 – 164.91	
Proximal femur BMD	0.989 ± 0.010	0.992 ± 0.010	0.980 ± 0.008	0.971 ± 0.009	0.46
Femoral neck BMD	0.780 ± 0.008	0.797 ± 0.009	0.787 ± 0.009	0.783 ± 0.008	0.48
Lumbar spine BMD	1.084 ± 0.018	1.091 ± 0.012	1.086 ± 0.017	1.072 ± 0.016	0.83
WOMEN					
n	222	222	210	253	
Dietary protein	51 ± 1	59 ± 2	69 ± 3	70 ± 2	
Dietary calcium	781 ± 26	782 ± 31	856 ± 54	687 ± 34	
Estimated NEAP range	8.42 – 34.93	34.99 – 46.74	46.78 – 58.44	58.49 – 162.32	
Proximal femur BMD	0.836 ± 0.008	0.823 ± 0.009	0.854 ± 0.010	0.849 ± 0.010	0.10
Femoral neck BMD	0.706 ± 0.008	0.696 ± 0.007	0.718 ± 0.009	0.722 ± 0.011	0.16

¹ NHANES = The National Health and Examination Survey

² Values are means ± SE

³ Values are least-squares means ± SE adjusted for age, height, weight, ethnicity, energy, physical activity, alcohol consumption, smoking status, caffeine intake, vitamin D supplement use, calcium supplement use, dietary calcium, dietary magnesium, hormone replacement therapy in women only

⁴ NEAP = estimated net endogenous acid production (mEq/d)

⁵ BMD = bone mineral density (g/cm²)

Table 3

Least square adjusted means and standard errors for BMD at proximal femur, femoral neck and lumbar spine by quartiles of estimated PRAL_{diet}, data from the NHANES years 2005–2008^{1–5}

	PRAL Quartile				p-trend
	1	2	3	4	
MEN					
n	285	269	318	346	
Dietary protein (g)	77 ± 2	73 ± 2	81 ± 3	95 ± 5	
Dietary calcium (mg)	1018 ± 39	856 ± 25	860 ± 45	877 ± 35	
Estimated PRAL range	-78.22, -1.16	-1.15, 8.62	8.64, 18.51	18.52, 69.96	
Proximal femur BMD	0.994 ± 0.008	0.989 ± 0.010	0.980 ± 0.008	0.970 ± 0.010	0.34
Femoral neck BMD	0.783 ± 0.007	0.797 ± 0.011	0.791 ± 0.009	0.776 ± 0.009	0.39
Lumbar spine BMD	1.081 ± 0.013	1.099 ± 0.017	1.076 ± 0.014	1.076 ± 0.014	0.57
WOMEN					
n	199	250	221	237	
Dietary protein (g)	56 ± 2	55 ± 1	61 ± 1	77 ± 3	
Dietary calcium (mg)	836 ± 33	725 ± 31	726 ± 23	820 ± 57	
Estimated PRAL range	-55.39, -5.66	-5.62, 3.60	3.61, 11.57	11.61, 49.53	
Proximal femur BMD	0.842 ± 0.008	0.821 ± 0.008	0.851 ± 0.010	0.847 ± 0.010	0.04*
Femoral neck BMD	0.706 ± 0.008	0.696 ± 0.007	0.717 ± 0.009	0.723 ± 0.010	0.16

¹The National Health and Nutrition Examination Survey

²Values are means ± SE

³Values are least-squares means ± SE adjusted for age, height, weight, ethnicity, energy, physical activity, alcohol consumption, smoking status, caffeine intake, vitamin D supplement use, hormone replacement therapy in women only

⁴PRAL = potential renal acid load (mEq/d) calculated from dietary calcium

⁵BMD = bone mineral density (g/cm²)

* Significant at the p<0.05 level.