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Food groups associated with measured net acid excretion in community-dwelling older adults

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Abstract

Background—Acid-producing diets have been associated with adverse health conditions. Dietary acid load can be estimated from dietary intake data, but the available methods require a full dietary assessment. We sought to identify a simpler means to estimate 24-hour urinary net acid excretion (NAE), a robust measure of net endogenous acid production, using self-reported intakes of fruits, vegetables (acid-neutralizing foods), grain and/or protein (acid-producing foods) acquired by two different methods in community-dwelling older adults. Identifying food groups associated with NAE using a method not requiring a full diet assessment could have a broad clinical application.

Methods—Fruit, vegetable, protein, and grain servings/day were estimated with a widely-used food frequency questionnaire (study A, n=162, 63±8 years). Differences in their intakes across NAE categories (<5, 5to <15, 15to <50, 50 milliequivalents (mEq)/day) were analyzed using analysis of variance. The findings were verified in a second study which estimated dietary intakes using a more detailed record-assisted 24- hour recall (study B, n=232, 67±6 years).

Results—Fruit intake was significantly associated with NAE in both studies. In study A, fruit intake was 9% lower with each categorical NAE increase (unstandardized beta=-0.21,p=0.01) and 7% lower with each categorical NAE increase in study B (unstandardized beta=-0.18;p=0.02). Grain intake was positively associated with NAE in study B only (unstandardized beta=+0.14;p=0.01). Vegetable and protein intake were not associated with NAE in either study.

Conclusion—The inverse association between fruit intake and NAE suggests low self-reported fruit intake may be an indicator of acid-producing diets in older adults.

Small disruptions in acid-base balance can be harmful to health (1;2). A higher acid load has been associated with several adverse health conditions including increased bone turnover and bone loss (3-5), impaired mobility and physical function (6-8), hypertension (9), and renal function decline (10;11). Not all studies have found similar associations with bone turnover (12;13) and hypertension (14), however. Acid-base homeostasis is readily modified by diet (2;15). The amounts of fruits and vegetables (acid-neutralizing foods) consumed relative to cereal grains and protein (acid-producing foods) influence net endogenous acid

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production (NEAP) and consequent metabolic acidosis (16). Western diets, which are lower in fruits and vegetables and higher in grains compared to current recommendations, are acid-producing (17-20).

NEAP reflects the balance between alkali- and acid- producing components of the diet and can be measured directly as 24-hour urinary net acid excretion (NAE) (21;22). Indirect methods to estimate NEAP based on dietary intakes have been developed (17;20;23). These calculations incorporate mineral and protein contents of foods, thus requiring access to food composition databases which may not be available or practical in many research or clinical settings. Our aim, therefore, was to identify the extent to which a single food group could provide a reasonable estimation of NAE using the servings per day of fruits, vegetables, grains, and protein self-reported using a food frequency questionnaire (FFQ). We then verified our findings in a second study that assessed dietary intake using a more detailed record-assisted 24-hour recall. In both studies we also calculated the estimated NEAP using the currently available method developed by Frassetto, which is based on potassium and protein intakes (23) and the potential renal acid load (PRAL) developed by Remer, which is based on protein, phosphorous, potassium, magnesium and calcium intakes (16).

Methods

Data were derived from two completed intervention trials of potassium bicarbonate in older community-dwelling adults, for which measures of NAE and dietary intakes were available at baseline (3;24). Both studies' recruitment and enrollment have been described in detail (3;24). Study A enrolled healthy free-living men and women between 50- 85 years of age with a glomerular filtration rate (GFR) of at least 50 ml/min/1.73m². Their mean BMI was 27.7kg/m² and 56% were female. All women were post-menopausal for at least 6 months. (24) Study B enrolled healthy, free-living men and women between 60-85 years old with a GFR of at least 50 ml/min/1.73m². Their mean BMI was 25.7kg/m² and 49% were female. All women were post-menopausal for at least one year (3). Both protocols were approved by the Institutional Review Board at Tufts Medical Center-Tufts University Health Sciences Campus and all participants provided written informed consent. Both studies are registered with clinicaltrials.gov (NCT1475214 and NCT00357214).

Dietary intakes

In study A dietary intakes over the previous 3 months were estimated using the Fred Hutchinson food frequency questionnaire (FFQ) (24;25). In study B dietary intakes were estimated using a record-assisted 24-hour recall on the day their NAE was measured (3). Study B subjects were provided with two-dimensional measuring aids to assist in portion-sizing and asked to briefly record everything they ate and drank along with supplements taken on a food log. Subjects could refer to their food log at the study visit the following day while a trained interviewer completed a 24-hour dietary recall with them. One participant in study A did not complete a FFQ and one participant in study B did not complete the record-assisted 24-hour recall at their baseline visits so were not included in this analysis. In both studies the Nutrition Data System for Research software version 2011 (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) was used to quantify the

servings per day of fruit, vegetable, protein, and grain groups according to the 2005 Dietary Guidelines for Americans. The foods included in these food groups are listed in Supplemental Table 1.

In both studies protein intake (grams/day), phosphorous intake (mg/d), potassium intake (mg/d), magnesium intake (mg/d), and calcium intake (mg/d) were estimated using the Nutrition Data System for Research software version 2011 as well. NEAP was calculated using the ratio of protein (grams per day) to potassium (mEq/day) according to Frassetto (NEAP = $-10.2 + 54.4(\text{grams protein per day} / \text{mEq potassium per day})$) (23). The PRAL was calculated according to Remer as $(0.49 * \text{protein g/d}) + (0.037 * \text{phosphorus mg/d}) - (0.021 * \text{potassium mg/d}) - (0.026 * \text{magnesium mg/d}) - (0.013 * \text{calcium mg/d})$ (16).

Biochemical analyses

In both studies, all participants collected their urine for 24 hours prior to their baseline visit. NAE (equal to titratable acid + $\text{NH}_4^+ - \text{HCO}_3^-$) was calculated using a modification of the titration method of Jorgensen (26), as described by Chan et al (27). Our laboratory's precision for this assay is 10.1% (24). Urinary creatinine was measured on an automated clinical chemistry analyzer (Olympus AU4000; Olympus America, Melville NY) with a 4% coefficient of variation (24).

Measurements

In both studies height was measured using a stadiometer and weight using a digital scale. Physical activity was estimated using the Physical Activity Scale for the Elderly (PASE) questionnaire (28). GFR was calculated using the 24-hour urine creatinine corrected for body surface area ($\text{ml/min}/1.73\text{m}^2$).

Statistical Approach

Studies A and B were analyzed separately using the same cross-sectional approach. The NAE was not normally distributed in either cohort and not amenable to a straightforward log transformation due to negative values. Therefore it was treated categorically as <5 , 5 to <15 , 15 to <50 and 50 mEq/ per day. These categories were chosen *a priori* based on our earlier study that found the largest reduction in bone resorption when a NAE < 5 mEq/d was achieved in response to 3 months of alkali supplementation. In the same study participants whose achieved NAE level was 15 mEq/d had smaller reductions in bone resorption (3). With the exception of the PRAL (based on the protein, phosphorous, potassium, magnesium, and calcium intake) which was normally distributed, all dietary intake measures and the NEAP (based on the ratio of potassium to protein) were transformed by taking the natural log to reduce skewness. In study B, a small constant (0.1) was added to fruit, vegetable, protein, and grain servings/day because a few participants reported not eating these food groups and zero values are not amenable to log transformation.

Participant characteristics were compared across NAE categories using analysis of variance (for continuous measures) or Cochran-Armitage trend test (for categorical measures). Analysis of variance was used to evaluate whether servings per day of fruit, vegetables,

grains, or protein differed according to NAE categories. We also evaluated whether animal or vegetable sources of protein are similarly associated with NAE. A parallel approach was used to evaluate the association of NAE with calculated NEAP and its components (protein and potassium intake) (23) and with calculated PRAL and its components (phosphorous, magnesium, calcium, in addition to protein and potassium intake) (16). In sensitivity analyses we adjusted all dietary variables for energy intake and also included gender and BMI as covariates (because BMI and gender were reported to differ according to dietary acid load (29;30) and dietary factors associated with NAE may also differ by gender and or BMI). Unadjusted values are presented throughout because these adjustments did not change the results appreciably. All analyses were carried out using SAS v9.3 (Cary, NC) and statistical significance was set at $p < 0.05$.

Results

The median (25, 75 percentile) NAE was 16.4 (8.3, 29.6) mEq/day in study A and 8.9 (3.4, 19.3) mEq/day in study B. Participant characteristics of both studies are shown according to NAE category in Table 1. In both studies there were more women in the lowest and more men in the highest NAE category (study A and study B p -trend < 0.01). Age, BMI, GFR, physical activity and race did not differ according to NAE category in either study. Energy intake (kcal/day) did not differ significantly across NAE categories in either study (both $p > 0.27$).

In study A, fruit intake was 9% lower with each categorical increase of NAE (Table 2; exponentiate -0.21; $p = 0.01$), but servings per day of grain, vegetables, and protein did not differ according to NAE category (all $p \geq 0.19$). The NEAP, based on the ratio of protein to potassium using the method of Frassetto, was 7% higher with each categorical increase in NAE (exponentiate 0.07; $p < 0.01$). The PRAL, which incorporates dietary protein, phosphorous, potassium, magnesium, and calcium intakes, was 2.8 mEq/day higher with each categorical increase in NAE ($p = 0.01$). When the components of the NEAP and PRAL equations were analyzed separately, potassium intake was 8% lower (exponentiate -0.08, $p = 0.04$) and magnesium intake was 9% lower (exponentiate -0.09, $p = 0.02$) with each increase in NAE category. Calcium and phosphorous intakes were not associated with NAE. The grams per day of protein also did not differ with NAE category. Neither animal nor vegetable protein intake was significantly associated with NAE when analyzed separately.

In study B, fruit intake was 7% lower with each categorical increase in NAE (Table 2; exponentiate -0.18, p -trend = 0.02). In this study, reported grain intake was 15% higher with each categorical increase in NAE (exponentiate 0.14, p -trend = 0), but the reported servings per day of vegetables and protein did not differ according to NAE category (both $p \geq 0.22$). NEAP (based on the ratio of protein to potassium intake) was 14% higher with each categorical increase in NAE (exponentiate 0.13, $p < 0.01$). The PRAL (based on dietary protein, phosphorous, potassium, magnesium, and calcium intakes) was 5.9 mEq/day higher with each categorical increase in NAE ($p = 0.01$). When the NEAP and PRAL equations' components were analyzed separately, potassium intake and magnesium intake were both 6% lower (exponentiate -0.06, $p = 0.03$) with each categorical increase in NAE. Calcium and phosphorous intakes were not associated with NAE. The grams/day of protein also did not

differ according to NAE category. Neither animal nor vegetable protein intake was significantly associated with NAE. The results of studies A and B were not changed when dietary intakes were adjusted to energy intake (kcal/day) (Supplemental Table 2). Inclusion of gender and BMI as covariates also did not appreciably change our results.

Discussion

We evaluated the association of NAE with self-reported servings per day of fruits, vegetables, grains and protein because these food groups make the largest dietary contribution to acid-base balance (16) and urine NAE is a direct and objective measure of endogenous acid production (16;23). Identifying acid-producing diets is important because acid-producing diets contribute to bone and muscle loss and kidney function decline (3-8;10;11), and can be readily modified. We found low fruit intake was associated with higher NAE in community-dwelling older adults and this was consistent whether dietary intakes were assessed by a commonly-used FFQ or a more rigorous record-assisted 24-hour recall. Fruits supply potassium and magnesium to the diet, which produce bicarbonate and other acid-neutralizing compounds as they are metabolized. Potassium and magnesium intake and fruit intake were similarly associated with NAE in both studies. In study A and study B potassium intake appeared to drive the association of the NEAP calculated according to Frassetto (23) with NAE. In addition to potassium intake, magnesium intake appeared to contribute to the association of the PRAL calculated according to Remer (16) with NAE. However, a full dietary assessment and access to nutrient databases are required to estimate intakes of potassium and other minerals to calculate NEAP and PRAL (16,23), while fruit intake can be estimated using simple questionnaires (which have been developed and validated (31;32)).

Vegetables are also alkali producers and higher intakes reduce NAE (16). However, we did not find higher self-reported vegetable intake to be associated with NAE in either of our studies. This may be related to reporting inaccuracies. A serving of vegetables was reported less correctly than a serving of fruit in Australians 16 years of age (33). When a short FFQ was used by older adults from the Netherlands, vegetable intake was overestimated by nearly 20% of respondents, while fruit intake was overestimated by less than 3% (34). Vegetables may be more difficult to quantify because they tend to be eaten as part of a meal, whereas fruit is more commonly consumed as one piece, which may be easier to count. Therefore querying vegetable intake does not appear to be a suitable means to screen older adults for acid-producing diets. We also acknowledge that the narrow range of vegetable intake may have limited our ability to identify an association with NAE.

Grains, like protein, are acid-producers (16;20;35). In a typical American diet (based on NHANES III) grains were reported to account for 38% of the dietary acid produced by acid-producing foods (20). Since the 1970s in the United States, the number of calories consumed as grains increased by 42% and in older adults, bread and grain desserts have now become the top contributors to energy intakes (18;19;36). Over the same time total energy intake increased, but protein intake remained constant (18;37). This suggests an increase in absolute grain consumption, which could promote an increase in dietary acid load in older adults. In a European adults (mean age 55 years), higher cereal grain intakes reported using

a FFQ were associated with lower (more acidic) urine pH in men, but not women (38). We found higher grain intakes were associated with higher NAE in study B but not study A, likely because study B utilized a more rigorous diet survey method and grain intake assessment on the same day as NAE was measured (3).

In contrast to other studies (16;17;23), protein intake, whether quantified as servings per day or grams per day (or grams/kilogram body weight/day (data not shown)), did not differ according to NAE in either of our studies. Protein intake was also not a significant contributor to the calculated NEAP (23) or PRAL (16) in either study. It is not clear why protein intake was a less important contributor to NAE and to NEAP and PRAL in our studies than it was in earlier studies (16;17;23). Limited variability in protein intake could explain a null association between it and NAE. Compared to studies that reported a positive association between protein intake and endogenous acid production, the variability in estimated protein intake in our studies was less than some (30;37), but similar to others (17;23;39). It is therefore questionable whether the protein intake variability is the only explanation for the null association between protein and NAE we observed. Another explanation is population differences. Our studies' participants were older than the majority of those studied previously (16;17;23). Alternatively, diet compositions may have been different, as discussed above. Animal- and plant- based protein may affect dietary acid load differently (20;40), but neither animal nor vegetable protein was associated significantly with NAE in either of our studies. The positive association between animal protein and NAE in study B approached statistical significance, which may suggest a larger sample size with a detailed dietary assessment is needed to better understand how animal- and plant- based sources of protein differentially influence NAE.

That self-reported fruit intake alone was consistently associated with NAE in our studies may reflect some of the bias' associated with self-reported dietary measures. For example, self-reported grain intakes were associated with higher NAE only when the record-assisted 24-hour recall was used. The failure of the FFQ method to identify grains as a significant contributor to NAE may be due, in part, to under-reporting. Study A participants in the highest NAE category reported consuming, on average, less than half the servings of grain per day than those in the same NAE category in study B (2.9 vs 6.3 serving/day, respectively). Under-reporting is further suggested by the fact that reported energy intakes were 25% lower in study A compared to study B, even though the BMI and reported physical activity were similar in both studies. We acknowledge this comparison is indirect because we compared the instruments across studies with different participants. However, a study that compared FFQs to recalls administered to the same individuals reported energy intake was 22-24% lower when the FFQ was used compared to the 24-hour recall (41). Similarly, in the Health Professionals Follow-up Study, refined grain intakes reported using a FFQ were 23% lower than when 7-day diet records were used (42). This underreporting may partially reflect social approval bias. This occurs when participants respond in manners more consistent to social norms than to what is true (43;44). While fruit intake may be easier to conceptualize and therefore reported with more accuracy than other food groups (33;34), social approval bias may lead to over-reporting of fruit as well (44), and this may have occurred in our studies. However, if fruit was over-reported, it appears to have been done so more consistently in the recall and food frequency methods and more consistently across

NAE categories, because lower self-reported fruit intake was associated with higher NAE in both of our studies.

Sub-clinical metabolic acidosis becomes more prevalent with age even in the absence of clinical disease(37). Therefore research on its health consequences is likely to focus on individuals similar to our studies' participants, although we acknowledge our findings may not be generalizable to younger or less healthy groups. In generally healthy older adults, we found low fruit intake was consistently associated with elevated NAE. This suggests obtaining information on older adults' fruit intake may provide an indication of their dietary acid load.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1
Participant characteristics according to net acid excretion category; mean (SD) unless otherwise indicated

	Net Acid Excretion, mEq/d			
	<5	5 to <15	15 to <50	50
Study AN	19	51	79	13
NAE, mEq/d (median (IQR))	1.9(4.3)	9.0(5.5)	25.0(13.1)	63.1(13.0)
Sex – n(%) female ^a	13(68)	35(69)	40(51)	4(31)
Race – n(%) white	19(100)	42(81)	68(86)	11(85)
Age, yr	66.9(8.3)	62.7(7.5)	62.6(7.7)	62.0(8.2)
BMI, kg/m ²	25.0(0.8)	25.5(0.5)	26.5(0.4)	26.6(1.0)
GFR, ml/min/1.73m ²	86.3(19.4)	91.1(24.1)	92.5(22.6)	100.9(25.4)
Physical Activity score	145(40)	166(78)	157(92)	217(72)
Dietary intakes				
Energy, kcal/day ^b	1273(111)	1530(82)	1467(63)	1269(135)
Fruit, servings/day ^{a,b}	2.7(1.6)	2.5(0.6)	1.9(0.3)	1.7(0.2)
Vegetable, servings/day ^b	2.9(0.4)	2.5(0.2)	2.5(0.2)	2.3(0.4)
Grain, servings/day ^b	3.5(0.5)	4.1(0.3)	3.7(0.2)	2.9(0.5)
Protein, servings/day ^b	3.4(0.4)	4.5(0.3)	4.5(0.3)	3.8(0.6)
Protein, g/day ^b	57.0(5.3)	67.7(3.9)	63.3(2.9)	52.6(6.0)
Animal protein, g/day ^b	38.5(4.0)	49.2(3.0)	46.1(2.3)	37.4(4.7)
Vegetable protein, g/day ^b	17.3(1.9)	16.4(1.1)	15.5(0.8)	13.8(1.8)
Phosphorous, mg/d ^{b,c}	1053 (495)	1200 (474)	1090 (458)	861 (349)
Potassium, mg/day ^{a,b,c}	2604(229)	2644(142)	2396(103)	2032(216)
Magnesium, mg/d ^{a,b,c}	273 (107)	272 (103)	250 (101)	198 (75)
Calcium, mg/d ^{b,c}	672 (430)	821 (402)	706 (367)	560 (218)
NEAP, mEq/d ^{a,b,d}	36.0 (8.1)	43.8 (10.6)	45.5 (11.8)	44.3 (11.8)
PRAL, mEq/d ^{a,e}	-3.6 (8.5)	4.3 (11.3)	5.9 (11.8)	4.3 (11.0)
Study B N	84	67	56	25
NAE, mEq/d (median (IQR))	2.4(2.6)	9.0(4.2)	20.8(16.2)	72.5(38.2)
Sex – n(%) female ^a	54 (65)	36 (54)	15 (27)	8 (32)
Race – n(%) white	77 (93)	61 (91)	51 (91)	23 (92)
Age, yr	66.4(4.9)	67.6(5.5)	67.5(6.3)	65.2(5.2)
BMI, kg/m ²	25.7(0.4)	25.8(0.5)	25.4(0.5)	26.0(0.8)
GFR, ml/min/1.73m ²	76.2(12.3)	75.8(14.0)	76.2(12.8)	75.7(10.2)
Physical Activity score	150(67)	131(61)	147(73)	155(95)
Dietary intakes				
Energy, kcal/day ^b	1865(71)	1882(81)	2044(96)	1916(135)
Fruit, servings/day ^{a b}	2.1(0.3)	1.6(0.2)	1.7(0.3)	1.0(0.3)

	Net Acid Excretion, mEq/d			
	<5	5 to <15	15 to <50	50
Vegetable, servings/day ^b	3.5(0.4)	3.2(0.4)	3.2(0.4)	2.6(0.5)
Grain, servings/day ^{a b}	4.0(0.4)	5.5(0.6)	5.1(0.6)	6.3(1.1)
Protein, servings/day ^b	4.4(0.5)	5.9(0.7)	4.5(0.7)	4.1(0.8)
Protein, g/day ^b	74.3(3.4)	82.7(4.2)	84.3(4.7)	75.8(6.3)
Animal protein, g/day ^b	32.3(3.6)	47.8(5.9)	42.3(5.3)	45.4(9.3)
Vegetable protein, g/day ^b	30.2(1.6)	27.6(1.7)	30.5(2.0)	27.2(2.7)
Phosphorous, mg/d ^{b,c}	1287 (533)	1308 (549)	1376 (677)	1198 (455)
Potassium, mg/day ^{a,b,c}	3248 (141)	3029 (148)	3138 (168)	2517 (199)
Magnesium, mg/d ^{a,b,c}	365 (163)	341 (141)	355 (150)	278 (108)
Calcium, mg/d ^{b,c}	925 (458)	857 (463)	922 (454)	829 (342)
NEAP, mEq/d ^{a,b,d}	34.9(2.5)	47.1(3.8)	45.9(4.0)	53.0(6.9)
PRAL, mEq/d ^{a,e}	-6.7 (31.7)	6.7 (19.8)	5.1 (27.0)	11.9 (19.6)

^a p-trend <0.05;

^b presented as geometric means(SEM; SEMs, were estimated using the delta method-(geometric mean)x(SEM of ln-transformed outcome).

^c mEq conversions: mEq potassium= mg/39, mEq calcium=(mg/40)*2, mEq phosphorous =(mg/31)*2, mEq magnesium= (mg/24.3)*2;

^d calculated as -10.2+(54.5(protein grams per day/potassium mEq per day))(23);

^e calculated as (0.49*protein g/d)+(0.037*phosphorus mg/d)-(0.021*potassium mg/d)-(0.026*magnesium mg/d)-(0.013*calcium mg/d) (16).

Table 2
Univariate associations of self-reported dietary intakes and net acid excretion category in older adults^{a,b}

	Study A (n=162)				Study B (n=232)			
	Unstandard beta (95%CI)	Standard beta	R ²	p-value	Unstandard beta (95%CI)	Standard beta	R ²	p-value
Fruits, servings/d	-0.21 (-0.38-0.04)	-0.19	0.035	0.01	-0.18 (-0.35 - -0.03)	-0.15	0.022	0.02
Vegetables, servings/d	-0.05 (-0.18-0.07)	-0.06	0.004	0.41	-0.08 (-0.20-0.05)	-0.08	0.006	0.22
Grains, servings/d	-0.06 (-0.18-0.05)	-0.09	0.008	0.19	0.14 (0.03-0.25)	0.16	0.026	0.01
Protein, servings/d	0.05 (-0.05-0.15)	0.08	0.006	0.34	-0.02 (-0.15-0.12)	-0.02	0.0003	0.80
Protein, g/d	-0.02 (-0.10-0.06)	-0.04	0.002	0.58	0.03 (-0.03-0.08)	0.07	0.005	0.30
Animal protein, g/d	-0.004 (-0.09 - 0.08)	-0.004	0.0001	0.92	0.12 (-0.01 - 0.25)	0.11	0.01	0.08
Vegetable protein, g/d	-0.07 (-0.16 - 0.03)	-0.05	0.01	0.16	-0.02 (-0.08 - 0.05)	-0.03	0.001	0.62
Potassium, mEq/d	-0.08 (-0.15 - -0.005)	-0.16	0.027	0.04	-0.06 (-0.11 - -0.01)	-0.06	0.020	0.03
Phosphorous, mEq/d	-0.05 (-0.14 - 0.03)	-0.05	0.011	0.19	-0.002 (-0.05 - 0.05)	-0.01	0.0001	0.93
Calcium, mEq/d	-0.07 (-0.17 - 0.03)	-0.10	0.011	0.19	-0.02 (-0.08 - 0.04)	-0.04	0.002	0.54
Magnesium, mEq/d	-0.09 (-0.16 - -0.01)	-0.18	0.032	0.02	-0.06 (-0.11 - -0.004)	-0.14	0.019	0.03
NEAP mEq/d ^c	0.07 (-0.02-0.12)	0.22	0.048	<0.01	0.13 (0.05-0.22)	0.20	0.041	<0.01
PRAL mEq/d ^d	2.77 (0.57-4.96)	0.19	0.037	0.01	5.88 (2.50-9.25)	0.22	0.049	<0.01

^a with exception of PRAL, all dietary measures were transformed using the natural log to reduce skewness;

^b analyzed using analysis of variance;

^c calculated as $-10.2 + (54.5 \times (\text{protein grams per day} / \text{potassium mEq per day}))$ (23);

^d calculated as $(0.49 \times \text{protein g/d}) + (0.037 \times \text{phosphorus mg/d}) - (0.021 \times \text{potassium mg/d}) - (0.026 \times \text{magnesium mg/d}) - (0.013 \times \text{calcium mg/d})$ (16).