Alkaline diets favor lean tissue mass in older adults[1–4]

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ABSTRACT

Background: Maintaining muscle mass while aging is important to prevent falls and fractures. Metabolic acidosis promotes muscle wasting, and the net acid load from diets that are rich in net acid–producing protein and cereal grains relative to their content of net alkali–producing fruit and vegetables may therefore contribute to a reduction in lean tissue mass in older adults.

Objective: We aimed to determine whether there was an association of 24-h urinary potassium and an index of fruit and vegetable content of the diet with the percentage lean body mass (%LBM) or change in %LBM in older subjects.

Design: Subjects were 384 men and women ≥65 y old who participated in a 3-y trial comparing calcium and vitamin D with placebo. Potassium was measured in 24-h urine collections at baseline. The %LBM, defined as total body nonfat, nonbone tissue weight ÷ weight × 100, was measured by using dual-energy X-ray absorptiometry at baseline and at 3 y. Physical activity, height, and weight were assessed at baseline and at 3 y.

Results: At baseline, the mean urinary potassium excretion was 67.0 ± 21.1 mmol/d. Urinary potassium (mmol/d) was significantly positively associated with %LBM at baseline ($\beta = 0.033$, $P = 0.006$; adjusted for sex, weight, and nitrogen excretion) but not with 3-y change in %LBM. Over the 3-y study, %LBM increased by 2.6 ± 3.6%.

Conclusion: Higher intake of foods rich in potassium, such as fruit and vegetables, may favor the preservation of muscle mass in older men and women. *Am J Clin Nutr* 2008;87:662–5.

KEY WORDS Urinary potassium, percentage lean body mass, humans

INTRODUCTION

Muscle mass gradually declines after age 50 y, and muscle loss leads to muscle weakness; greater risks of falls, fractures, and disability; and loss of independence (1–4). The cause of age-related muscle loss is multifactorial, but there is plausible evidence that the composition of diets with respect to acid-base balance is a contributing factor. Protein and cereal grains are metabolized to acidic residues, mainly sulfuric acid, and fruit and vegetables are metabolized to alkaline residues, mainly potassium bicarbonate. In general, American diets are acidogenic, generating 75–100 mEq acid/d (5). With the decline in renal function that occurs with aging (6), older persons are not able to excrete the excess hydrogen ions, and they develop mild but slowly increasing metabolic acidosis (7).

Metabolic acidosis has been linked to muscle wasting in chronic renal failure (8) and in obese subjects who were acidotic while following weight-loss diets (9, 10); correction of the acidosis has been shown to reverse the muscle wasting in these 2 conditions (11, 12). In a short-term metabolic study in 14 healthy postmenopausal women following isocaloric, acidogenic high-protein metabolic diets, the ingestion of a neutralizing dose of potassium bicarbonate significantly reduced nitrogen excretion over an 18-d period (13). Muscle wasting appears to be an adaptive response to acidosis (14–17). With muscle breakdown, amino acids are released into the bloodstream. These amino acids provide a substrate for the hepatic synthesis of glutamine. Glutamine is used by the kidney to synthesize ammonia (18). Ammonia molecules spontaneously accept protons and are excreted as ammonium ions; the excretion of ammonium thus removes protons and mitigates the acidosis. The objectives of the present study were to investigate associations of 24-h urinary potassium with percentage lean body mass (%LBM) and with the 3-y change in %LBM in 384 healthy men and women ≥65 y old who were consuming their usual diets.

SUBJECTS AND METHODS

Subjects and study design

The 384 subjects in this study (172 M, 212 F) were among the 389 subjects who completed the National Institute on Aging Sites Testing Osteoporosis Prevention/Intervention Treatment (STOP/IT) trial at Tufts University. In that 3-y study, subjects were randomly assigned to treatment with calcium (500 mg as citrate malate) plus vitamin D_3 (700 IU) or double placebo. Exclusion criteria were osteoporosis medications or hormone replacement in the past 2 y, glucocorticoid use in the past 6 mo, serum creatinine > 1.2 mg/dL (>106.1 μmol/L), liver disease, current cancer, and hyperparathyroidism. Exclusion criteria were published previously (19).

In the cross-sectional analyses, 2 subjects were omitted for missing urinary potassium measurements, 2 for missing physical

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activity measurements, and one for missing a dual-energy X-ray absorptiometry (DXA) scan. In the longitudinal analyses, 3 additional subjects were omitted for missing 3-y DXA measurements.

Written informed consent was obtained from all subjects. The study protocol was approved by the Investigational Review Board at Tufts University.

Measurements

Throughout the trial, subjects came to the center every 6 mo for follow-up visits. Data gathered on the baseline and final (3-y) visits are the subject of this analysis. Physical activity including leisure, household, and occupational activity was estimated at baseline and at 3 y by using the Physical Activity Scale for the Elderly questionnaire (20). Weight was measured on a digital scale while subjects were wearing light clothing, and height was measured with the use of a stadiometer. Protein and potassium intake over the previous 6 mo was estimated at the 18-mo visit by using Willett's food-frequency questionnaire (21).

LBM was measured by using DXA on a Prodigy scanner (GE-Lunar, Madison, WI) and with the use of GE-LUNAR software (version 5.0; GE-Lunar). The CV of lean tissue mass measurements in our laboratory is 0.77% (22). The %LBM was calculated as the weight of lean tissue ÷ weight × 100.

Fasting serum creatinine was measured by using colorimetry and plasma 25-hydroxyvitamin D was measured by using a competitive protein-binding method as previously described (19). All urine measurements were made on aliquots of 24-h urine collections. Urinary potassium and creatinine were measured by direct-current plasma emission spectroscopy with the use of a Spectraspan 6 (Beckman Instruments, Palo Alto, CA); intraassay and interassay CVs were 2.7% and 6.8%, respectively. Creatinine clearance was computed and adjusted for body surface area. Urinary nitrogen was measured with the use of a nitrogen-protein determinator (model FP-2000: LECO, St. Joseph, MI). This instrument uses a Dumas combustion method (23) and performs detection with the use of a thermal conductivity cell. It measures nitrogen with a precision of 15 ppm.

Statistical analysis

Analyses were conducted with SPSS software (version 14.0; SPSS Inc, Chicago, IL). Two-tailed P values < 0.05 were considered to indicate significance. Data were reviewed graphically for evidence of outliers and nonnormality. Partial correlations and analysis of covariance were used to evaluate linear associations of nitrogen and potassium with %LBM and changes in %LBM after adjustment for covariates. In preliminary analyses, the possible influence of sex on these associations was investigated by including interaction terms in the analysis of covariance models; because these terms were not statistically significant ($P > 0.26$), subsequent analyses were conducted in the pooled sample.

RESULTS

The clinical and laboratory characteristics of the 384 subjects are shown in **Table 1**. The group was of relatively high socioeconomic status, as indicated by their level of education. Over the 3-y study, 48.4% of the subjects were treated with calcium and vitamin D, and the remainder received placebo. Mean creatinine clearance was 86.5 ± 20.9 mL/min, but 28 subjects had clearance rates < 60 mL/min.

TABLE 1
Baseline clinical and laboratory characteristics of study subjects[1]

Characteristics	Value
Age (y)	71.0 ± 4.6[2]
Weight by digital scale (kg)	74.2 ± 14.1
Height (cm)	165.9 ± 9.7
BMI (kg/cm^2)	26.8 ± 4.1
PASE score	114.8 ± 55.2
Attended college (%)	74.2
Diuretic user (%)	11.5
Male (%)	45
Serum 25(OH)D (nmol/L)	74.0 ± 34.3
24-hr Urine	
Potassium (mmol)	67.0 ± 21.1
Nitrogen (mmoL)	770 ± 251
Creatinine (mmol/d)	10.2 ± 3.3
Creatinine clearance (mL/min)	86.5 ± 20.9
Total tissue weight by DXA (kg)	73.1 ± 14.2
Lean body mass by DXA (kg)	45.3 ± 10.0

[1] $n = 384$. PASE, Physical Activity Scale for the Elderly; 25(OH)D, 25-hydroxyvitamin D; DXA, dual-energy X-ray absorptiometry.
[2] $\bar{x}$ ± SD (all such values).

Protein intake was not assessed at baseline but, at the 18-mo visit, the mean ± SD value was 80.0 ± 29.4 g/d ($n = 339$). Also at the 18-mo visit, mean potassium intake was 3540 ± 1196 mg/d (range: 1062–10 698 mg/d). Fruit (25.9%) and vegetables (18.7%) were the 2 major sources, accounting for 44.6% of total potassium intake. Other components were grains and starches (16.5%), dairy (14.4%), meat and eggs (12.0%), beverages (7.4%), and sweets (5.0%). Urinary potassium was significantly correlated with LBM ($r = 0.34$, $P < 0.001$) but not with fat tissue mass ($r = 0.00$, $P = 1.0$).

Urinary potassium and percentage lean body mass at baseline

Variables associated with both potassium excretion and %LBM were considered as potential confounders of the association between potassium and %LBM. Continuous variables in this category were identified by computing their partial correlations, after adjustment for sex, with potassium and %LBM (**Table 2**). Weight and nitrogen excretion clearly needed to be adjusted for because of a strong correlation with %LBM (weight) or potassium excretion (nitrogen) and at least a weak association with the other variable (ie, %LBM or nitrogen). Results of regression analyses in which only these 2 variables and sex are adjusted for, the "minimally adjusted" model, are shown in **Table 3** (model 2). In a third, "fully adjusted" model, we also adjusted for variables that were correlated ($r = \geq 0.08$) with potassium excretion only (ie, creatinine clearance and activity score) or %LBM only (ie, age and 25-hydrovitamin D), even if those correlations were not significant at the 0.05 level. Finally, we added the use of diuretics (yes or no) to this model because diuretic users had significantly $P = 0.045$) lower %LBM than did nonusers (58.9 ± 7.2 and 61.6 ± 8.3, respectively). As expected from the way those factors were selected, adjustment for sex, body weight, and nitrogen excretion had an important effect on the regression coefficient for potassium excretion (change from

TABLE 2
Sex-adjusted correlations of potential confounders with potassium excretion and percentage lean body mass (%LBM)[1]

	Potassium excretion		%LBM	
	r	*P*	*r*	*P*
Age	−0.04	0.426	0.14	0.006
Weight	0.16	0.002	−0.71	<0.001
Activity score	0.08	0.133	0.04	0.475
Nitrogen excretion	0.54	<0.001	−0.13	0.009
Creatinine clearance	0.34	<0.001	0.07	0.157
25(OH)D	0.07	0.173	0.11	0.034

[1] 25(OH)D, 25-hydroxyvitamin D.

model 1 to model 2), but further adjustments did not (change from model 2 to model 3).

There was no significant interaction with nitrogen in the association of urinary potassium with %LBM (P for interaction = 0.861). Urinary potassium and nitrogen were positively correlated ($r = 0.524$, $P < 0.001$). The association of potassium with %LBM in the men and the women, divided into quartiles of adjusted mean potassium (adjustments in model 2), is shown in **Figure 1**. Although men had greater %LBM than the women, the association of potassium with %LBM did not differ significantly between the men and the women.

Urinary potassium and 3-y change in percentage lean body mass

The 24-h urinary potassium was not significantly associated with 3-y change in %LBM either before or after adjustment for sex, weight, baseline LBM, nitrogen excretion, and treatment group ($\beta = 0.001$, $P = 0.910$). Baseline urinary nitrogen also was not significantly associated with 3-y change in %LBM ($\beta < 0.001$, $P = 0.987$).

Over the 3-y study period, weight measured by digital scale decreased by 0.60 ± 3.93 kg, and the change did not differ significantly between the 2 treatment groups. Over the same period, DXA-measured total tissue weight increased by 0.47 ± 3.9 kg. Weights obtained by these 2 measurements were highly correlated ($r = 0.933$, $P < 0.001$). LBM increased by 1.38 ± 1.66 kg, and %LBM increased by 2.6 ± 3.6%.

TABLE 3
Regressions of percentage lean body mass on urinary potassium excretion[1]

	β	*P*
Model 1 (unadjusted)		
Potassium excretion (mmol/d)	0.077	<0.001
Model 2 (minimally adjusted)		
Potassium excretion (mmol/d)	0.033	0.006
Sex (% male)	15.843	<0.001
Body weight (kg)	−0.377	<0.001
Nitrogen excretion (mmol/d)	0.002	0.048
Model 3 (fully adjusted)		
Potassium excretion (mmol/d)	0.031	0.013
Sex (% male)	15.683	<0.001
Body weight (kg)	−0.368	<0.001
Nitrogen excretion (mmol/d)	0.001	0.342
Age (y)	0.054	0.271
Activity score	0.007	0.095
Creatinine clearance (mL/min)	0.022	0.085
25(OH)D (nmol/L)	<0.001	0.976
Diuretic use (yes)	−0.178	0.768

[1] 25(OH)D, 25-hydroxyvitamin D.

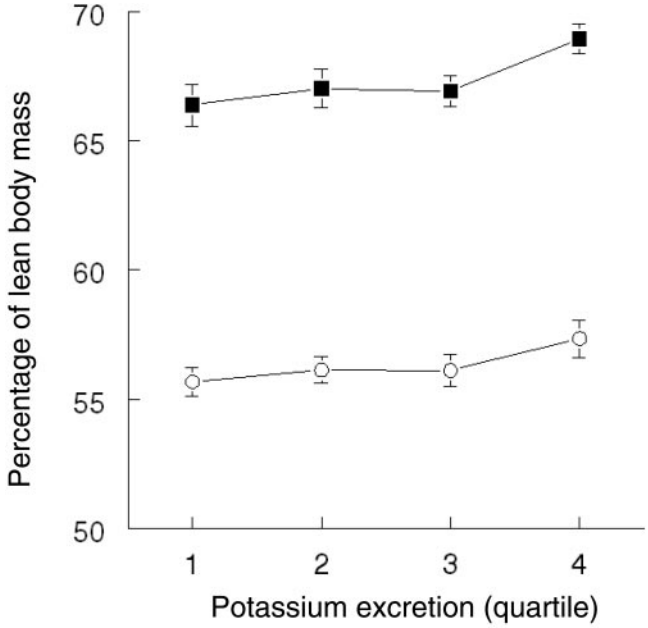

FIGURE 1. Associations between quartile of potassium excretion and percentage lean body mass after adjustment for weight and nitrogen excretion in the 172 men (■) and 212 women (○). The quartile boundaries of potassium excretion were 52.3, 64.9, and 81.0 mmol/d.

DISCUSSION

This study indicates that higher excretion of potassium, a reflection of greater potassium intake, is associated with greater %LBM in healthy older men and women. The significant correlation of urinary potassium with lean mass but not with fat mass suggests that potassium is acting on lean rather than on fat tissue. The positive association of potassium with %LBM may be related to the neutralizing effect of increased ingestion of potassium salts on the mild metabolic acidosis resulting from habitual ingestion of a typical net acid–producing American diet. Several studies have shown that metabolic acidosis promotes nitrogen excretion, or muscle wasting. In rats, metabolic acidosis induced by the ingestion of 8 mmol hydrochloric acid·100 g $wt^{-1} \cdot d^{-1}$ significantly increased urinary total nitrogen excretion (14). The nitrogen wasting increased significantly by day 10 and persisted over the 15-d study period. The acid load given was sufficient to lower serum bicarbonate from 27.19 to 18.97 mmol/L but not sufficient to cause any notable gastrointestinal disturbance or decrease in food intake. There is evidence from an 18-d study in humans that the administration of alkaline salts may have a favorable effect on muscle mass, at least acutely (13). Frassetto et al (13) found that oral administration of 90 mmol K/d promptly reduced nitrogen excretion from 14.0 ± 0.6 to 13.2 ± 0.5 g/d ($P < 0.001$) in 14 healthy postmenopausal women who were following acidogenic (high-protein) metabolic diets. In these subjects who were studied on fixed protein intakes and under constant exercise conditions, the decline in nitrogen excretion was interpreted as conservation of skeletal muscle mass.

According to their urinary potassium and because 90% of the potassium in the diet is excreted by the kidneys (24), the subjects in this study were consuming amounts of potassium that are typical for adults in the United States and that are approximately one-half of the amounts recommended by the Institute of Medicine (25). Our findings from model 2 indicate that subjects with a potassium intake of 134 mmol/d can expect to have 1.64 kg more lean tissue mass than subjects with half that potassium intake. That measure is almost as great as the amount of lean tissue that is typically lost in a decade in an older population—ie, 2 kg. Extrapolating from their data, Frassetto et al (13) calculated that treatment with 90 mmol $KHCO_3$/d theoretically could more than offset the chronic losses of muscle mass that occur over time and that result in sarcopenia. Our findings, using a very different approach, are consistent with the conclusion of Frassetto et al that much of the loss of lean tissue mass that occurs with aging can likely be prevented by increasing the intake of alkaline potassium salts to the recommended level.

The finding that total tissue weight measured by DXA increased by 0.5 kg over the 3-y study is unexpected, in view of the fact that, with the use of a digital scale, weight decreased by 0.6 kg. This difference suggests that there may have been some drift in absolute measurements of tissue weight by DXA, despite stable weekly phantom scans during the trial (19), and this possibility may explain the measured increase in LBM in a population that would be expected to lose muscle mass over 3 y (13). However, even if absolute measurements of LBM were affected in this way, we would expect the ranking of subjects with respect to their %LBM and changes in %LBM to be unaffected and, therefore, the estimated associations of urinary potassium with %LBM and changes in %LBM to be valid.

The present study had limitations. The diet data were collected at the 18-mo visit, not at baseline, and we have only one baseline measure of potassium excretion. We do not have verification (by using para-aminobenzoic acid or other means) that the 24-h urine collections are complete, but we have no reason to think that completeness of the collections would vary with %LBM. The positive findings linking potassium excretion and %LBM are restricted to the cross-sectional analyses. It will be important to determine prospectively the effect of the increasing intake of net alkali–producing foods on muscle mass and function.

In conclusion, our findings indicate that a higher potassium excretion, an index of alkaline potassium salt intake, is associated with a higher %LBM in healthy older men and women. This association is likely to result from the fact that the ingestion of potassium-rich alkaline foods such as fruit and vegetables relieves the mild metabolic acidosis that occurs with the ingestion of a typical American diet that is rich in protein, cereal grains, and other net acid–producing foods.

The author's responsibilities were as follows—BDH: principal investigator and manuscript preparation; SSH: data analysis and manuscript preparation; and LC: data interpretation and manuscript preparation. None of the authors was affiliated in any way with any entity involved in the manufacture of products related to muscle mass or alkaline salts. BDH has served on scientific advisory boards for Lilly, Procter and Gamble, Merck, and GlaxoSmithKline.

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