

A higher alkaline dietary load is associated with greater indexes of skeletal muscle mass in women

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Abstract

Summary Conservation of muscle mass is important for fall and fracture prevention but further understanding of the causes of age-related muscle loss is required. This study found a more alkaline diet was positively associated with muscle mass in women suggesting a role for dietary acid–base load in muscle loss.

Introduction Conservation of skeletal muscle is important for preventing falls and fractures but age-related loss of muscle mass occurs even in healthy individuals. However, the mild metabolic acidosis associated with an acidogenic dietary acid–base load could influence loss of muscle mass.

Methods We investigated the association between fat-free mass (FFM), percentage FFM (FFM%) and fat-free mass index (FFMI, weight/height²), measured using dual-energy X-ray absorptiometry in 2,689 women aged 18–79 years from the TwinsUK Study, and dietary acid–base load. Body composition was calculated according to quartile of potential renal acid load and adjusted for age, physical activity, misreporting and smoking habit (FFM, FFMI also for fat mass) and additionally with percentage protein.

Results Fat-free mass was positively associated with a more alkalinogenic dietary load (comparing quartile 1 vs 4: FFM 0.79 kg $P < 0.001$, FFM% 1.06 % < 0.001 , FFMI 0.24 kg/m² $P = 0.002$), and with the ratio of fruits and vegetables to potential acidogenic foods.

Conclusions We observed a small but significant positive association between a more alkaline diet and muscle mass indexes in healthy women that was independent of age, physical activity and protein intake equating to a scale of effect between a fifth and one half of the observed relationship with 10 years of age. Although protein is important for maintenance of muscle mass, eating fruits and vegetables that supply adequate amounts of potassium and magnesium are also relevant. The results suggest a potential role for diet in the prevention of muscle loss.

Keywords Diet acid–base Load · Fat-free mass · Muscle · Potential renal acid load (PRAL) · Sarcopenia

Introduction

Skeletal muscle is required to maintain posture and mobility [1]. However, there is loss of muscle mass and strength (sarcopenia) which starts even in healthy individuals from the age of 40 that is a major contributor to loss of functional ability and increased frailty in the elderly [2, 3]. Fractures and falls are a major public health problem costing £2.3 billion per year in health and social care in the UK alone, and \$17 billion per year in the USA therefore, methods of preventing them are required [4, 5]. Conservation of skeletal muscle mass is important in preventing falls and fractures as it is positively associated with bone density and, in addition to its role in maintaining balance, may also act as a protective barrier to reduce the impact of falls [6–9]. Despite the importance of skeletal muscle, at present, the causes of muscle loss in the healthy population are incompletely understood [10].

The metabolic acidosis associated with chronic kidney disease is a major cause of skeletal muscle mass loss in that condition, with reversal of muscle loss associated with

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correction of acidosis [11, 12]. However, the potential for mild metabolic acidosis associated with an acidogenic dietary acid–base load to influence muscle loss has been less well studied.

Nutrition is important in muscle metabolism with protein integral to muscle composition and function and there is some evidence that vitamin D is relevant to function and muscle mass [13, 3]. A deficit in protein will lead to a negative nitrogen balance and loss of skeletal muscle mass [3, 14–16]. However, although adequate protein is required for the prevention and management of sarcopenia the optimum quantities are under debate, particularly in older people [3, 14–16].

Dietary acid–base load consists of the contribution from both acidogenic and alkaligenic forming foods. Protein containing foods, including meats, fish, eggs, cereals and dairy foods are acidogenic as metabolism by the liver of the sulphur containing amino acids (cysteine and methionine) results in the production of hydrogen ions which can lower blood pH [17–19]. Alkaligenic foods balance the mild metabolic acidosis from metabolism of acidogenic foods via the carbonate present as alkaline salts in fruits and vegetables [17–19]. Dietary acid–base load is a balance between acidogenic foods (protein containing foods) and alkaligenic foods (fruits and vegetables) that supply base precursors.

Evidence for the metabolic effects of dietary acid–base load exists since the relationship with Net Acid Excretion and urine pH has been demonstrated in population and intervention studies [17–19]. Previously, a more acidic dietary acid–base load has been related to the skeletal system, with lower bone density in women and children associated with a more acidic dietary load, although recent intervention studies with alkaline salts found mixed effects on markers on bone turnover [20–24]. However, to date, the effects of mild metabolic acidosis on muscle mass in healthy participants have only been investigated in a few studies of middle- and older-aged populations [11, 24–26]. Acidosis may impact on the loss of muscle mass through effects on protein metabolism by decreasing synthesis and accelerating proteolysis and amino acid oxidation, mediated via the ubiquitin proteasome system the major pathway degrading protein in skeletal muscle, or via alterations in IGF-1 signalling [26, 27].

One measure of the balance between acidogenic and alkaligenic foods is the potential renal acid load (PRAL) which includes contributions from nutrient categories that relate to the major determinants of their acid or base forming potential, i.e. protein and phosphorus (acidogenic) and calcium, potassium and magnesium (alkaligenic) [17–19].

The purpose of this study was to investigate the association between dietary acid–base load, as estimated by PRAL, and fat-free mass measured using dual-energy X-

ray absorptiometry (DXA) body scans in a cohort of healthy women with a wide range of ages to further understand the effects of diet in the loss and maintenance of muscle mass.

Materials and methods

Subjects and study design

The TwinsUK Registry is an on-going study of healthy adult twin volunteers who have undergone extensive clinical assessments to collect data for a range of age-related characteristics [28]. The data includes information from registered twins who were sent questionnaires concerning health and lifestyle behaviours and who had physical assessments. This study included 2689 of the female twins aged 18–79 years who had complete data for DXA body scans, dietary questionnaires and clinical assessments between 1996 and 2000. The participants in the study were not selected for any characteristic or disease trait. Participants in the TwinsUK Registry have been shown to be representative of adult singleton populations in the UK [29, 30].

Zygosity was derived by questionnaire and confirmed by multiplex-DNA fingerprinting (PE Applied Biosystems). Physical activity during work and leisure time was derived by questionnaire using the Allied Dunbar Physical Activity Score as inactive, light, moderate and heavy exercise [31]. Smoking habit was determined from questionnaire as current, ex- or never smoker. Ethical approval was obtained from the St. Thomas's Hospital Research Ethics committee and informed consent was obtained from all subjects.

Assessment of body composition

Height and weight were measured using standard scales and BMI calculated by dividing weight (in kilograms) by the square of height (in meters). Body composition was measured using dual-energy X-ray absorptiometry (Hologic QDR) with participants in a supine position on the table top with their feet in a neutral position and hands flat by their sides. Total fat mass and fat-free mass were determined using standard software calculations. Percentage fat-free mass (FFM%) was calculated as: $\text{FFM kg}/\text{total body weight} \times 100$. Fat-free mass index (FFMI) was calculated as: $\text{FFM kg}/\text{height}^2$ [32].

Dietary intake

Dietary intake was calculated using a validated 131 item semi-quantitative Food Frequency Questionnaire (FFQ), previously used in the EPIC-Norfolk (European Prospective Investigations into Cancer and Nutrition) study which is as valid for PRAL when compared with 24-h urine pH as other

more detailed dietary methods [17, 30, 33, 34]. Subjects completed the frequency of consumption of foods which were described in average portion sizes. Nutrients were calculated using the UK National Nutrient Database [33, 34]. Individuals were excluded, a priori, if more than 10 items on the FFQ were left blank or if the ratio of energy intakes to estimated basal metabolic rate were >2 standard deviations from the mean of the ratio [30, 33].

$$\text{PRAL (in milliequivalents/day)} = (\text{milligrams phosphorus/day} \times 0.0366) + (\text{grams protein/day} \times 0.4888) \\ - (\text{milligrams potassium/day} \times 0.0205) + (\text{milligrams calcium/day} \times 0.0125) + (\text{milligrams magnesium/day} \times 0.0263)$$

The protein/potassium ratio was calculated as: protein grams/day/potassium in milliequivalents. Percentage protein intake was calculated as protein in grams/day \times 4 kcal and divided by total energy intake in kilocalories.

Statistical methods

Statistical analyses were performed with Stata statistical software version 11.0 (Stata Corp, College Station, TX). Quartiles of PRAL intake were calculated (quartile 1 being more alkaline, quartile 4 being more acidic.). Means and standard deviation of FFM, FFM% and FFMI were calculated for quartiles of dietary PRAL intake. Since the proportion of fat-free mass is negatively influenced by age, smoking habit and physical activity, these covariates were included in the models [37–40]. As in addition to total body weight, total fat mass also influences the total amount of fat-free mass the models for FFM and FFMI were also adjusted for fat mass (FFM% is a measure that is proportional to fat mass) [32]. To account for potential effects of differences in dietary reporting habit (misreporting) we also included the EI:EER in the models [36]. Additionally, since protein is also involved in muscle metabolism, we included percentage protein in the final model [3]. Three models are presented in the tables; model 1 unadjusted data; model 2 adjusted for age, physical activity, EI:EER and smoking habit and in the case of FFM and FFMI also for total fat mass; model 3 included the covariates as in model 2 but also included percentage protein intake. The analyses were also repeated with the protein/potassium ratio.

To determine whether there might be a different association between PRAL and FFM in relation to menopausal status, we repeated the analyses stratified by age, those above and those below the age of 55 years.

To further understand the relationship between the foods contributing to PRAL and their proportion in the diet, the ratio of the proportion of fruit and vegetable (alkalinogenic) foods to other potentially acidogenic forming foods in the

To estimate energy requirements the ratio of reported energy intake (EI:EER) to estimated energy expenditure was calculated and this was included as a covariate for adjustment in the statistical analyses [35, 36].

The measure of dietary acid–base load used was the PRAL index which was calculated by using individual nutrients derived from the FFQ using the following formula [18, 23]:

diet was derived: the proportion of fruits and vegetables to the total amount of all potentially acid forming foods; meats, fish, dairy foods, eggs and cereal foods (FNVEG: PROT CER). The ratio was divided into quartiles (Q1 representing the lowest proportion of fruit and vegetables to diet and Q4 representing the greatest proportion of fruit and vegetables to diet) and the mean and standard deviation of FFM, FFM%, and FFMI then calculated according to quartile. Adjustment for covariates was performed as for model 2 above. As data from members of twin pairs could not be treated as independent we controlled for familial aggregation by treating twin pairs as clusters by using the robust regression cluster option in Stata software. Models were also run either including zygosity as a covariate or stratified by zygosity. Within-pair models were also run.

The contribution to potassium intake of different food types was calculated.

Results

Our cohort of 2,689 female twins ranged from 18–79 years with 50 % of the group aged 50 years or more, Table 1. Around three quarters of the sample reported moderate or heavy physical activity and 18.7 % were current smokers. Within the cohort, 1,818 were dizygotic twins and 796 were monozygotic. The mean SD protein intake per kilogram body weight was 1.26 g/kg (0.37) (the US RDA for protein for women in the age group 18–75 years and over is 0.80 g/kg/day) [35].

Mean intake of PRAL was -9.24 mEq/day (SD 11.94) and ranged from -24.44 mEq/day in quartile 1 (most alkaline) to 4.83 mEq/day in quartile 4 (most acidic), a difference of 29.27 mEq/day, Table 2. Only age and physical activity were significantly related to quartiles of a more acidic PRAL intake. Protein intake was negatively associated with a more alkaline PRAL ($P < 0.001$) while magnesium and potassium were positively related to a more alkaline

Table 1 Characteristics of the study population of 2,689 women aged 18–79 years

	Mean	SD
<i>N</i> (2689)		
Age, years	48.2	12.7
Height, cm	162.4	6.0
Weight, kg	65.6	11.3
BMI, kg/m ²	24.9	4.2
Fat mass, kg	22.8	7.9
FFM, kg	39.6	5.3
FFM%, %	61.0	6.5
FFMI, kg/m ²	15.0	1.7
Current smokers, % (<i>N</i>)	18.7 (494)	
Physical activity, % active (<i>N</i>)	78.0 (2097)	
PRAL, mEq/day	-9.24	11.94
Nutrients		
Energy, kcal/d	1977	526
Protein, g/day	81.1	21.5
Protein, % energy	16.6	2.6
Phosphorus, mg/day	1518	409
Calcium, mg/day	1132	374
Potassium, mg/day	3963	1000
Magnesium, mg/day	343	92.4
Protein g/kg body weight	1.26	0.37
Foods		
Meat, g/day	93.2	50.7
Fish, g/day	35.1	25.8
Eggs, g/day	10.4	10.2
Cereals, g/day	265	114
Dairy, g/day	425	202
Fruit, g/day	246	192
Vegetables, g/day	324	161
FNVEG:PROTCER	0.75	0.48

Values are mean, SD unless stated otherwise

Meat (meats and meat products), dairy (all dairy, milk, yogurt, cream, cheese), cereals (all breads, cakes, biscuits, rice, pasta). FNVEG:PROTCER the proportion of fruits and vegetables to the total amount of meats, fish, dairy foods, eggs, and cereal foods

FFM fat-free mass (kilogram), FFM% percentage fat-free mass (percent), FFMI fat-free mass index (kilograms per square meter), PRAL potential renal acid load

PRAL ($P < 0.001$) with calcium and phosphorus not significantly related. Energy intake was not significantly associated with PRAL ($r = 0.028$, $P = 0.281$). Intakes of foods negatively and significantly associated with a more alkaline PRAL were meat, fish and cereals, all $P < 0.001$ and eggs $P = 0.007$, whereas fruit and vegetables were positively related to a more alkaline PRAL $P < 0.001$. The main foods that contributed to 62 % of potassium intake were fruit and vegetables (30.2 %), dairy foods (17.3 %) and potatoes (14.4 %).

Table 3 summarises the three models derived to examine for the association between acid–base load and fat-free mass. Total FFM was 0.45 kg higher in those eating a more alkaline diet (quartile 1 of PRAL) than in those eating a more acidic diet (quartile 4 of PRAL), in the unadjusted model and 0.79 kg higher in the adjusted model. The trend was not significant in the unadjusted model but was significant after adjustment for age, physical activity, EI:EER, smoking and fat mass ($P = 0.001$). Further adjustment for percentage protein intake did not materially change the association ($P = 0.010$). There was also a trend towards a difference in FFM% of 0.47 % ($P = 0.18$) with a more acidic diet but this was not statistically significant. The difference was greater (1.06 %) and significant ($P < 0.001$) after adjustment for age, physical activity and smoking and also remained significant with further adjustment for percentage protein intake ($P = 0.008$). The FFMI was significantly lower with a more acidic diet both with and without adjustment for age, EI:EER, physical activity, smoking and fat mass: 0.2 kg/m² ($P = 0.040$) and 0.24 kg/m² ($P = 0.002$) (Table 3). After adjustment for percentage protein the association between FFMI and acid–base load was greater, a difference of 0.28 kg/m² ($P = 0.001$). When compared with the mean value for the whole cohort the differences between quartile 1 and quartile 4 ranged between 1.6 and 2.0 % of the adjusted mean for FFMI and FFM, respectively, and after adjustment for protein intake were between 1.3 and 1.9 % for FFM% and the FFMI, respectively (Table 3). The associations found did not differ substantially by menopausal status (above and below the age of 55 years) data not shown. In addition the association between the protein/potassium ratio and the indexes of skeletal muscle mass did not differ substantially from the results with PRAL, data not shown. Also the results did not differ by zygosity.

For indexes of fat-free mass (FFM, FFM%, FFMI), our data suggest that a one quartile increase in PRAL was associated with a 0.28 kg negative difference in FFM ($P = 0.001$), a 0.37 % difference in FFM% ($P < 0.001$), and a 0.09 kg/m² difference in FFMI ($P = 0.002$), Table 4. After further adjustment for percentage protein intake, the associations were attenuated for FFM and FFM% and increased for FFMI. Percentage protein was not significantly associated with FFMI but was negatively associated with FFM% ($P = 0.031$) and there was a trend towards significance with FFM ($P = 0.09$). Compared with PRAL, the association between indexes of fat-free mass with smoking were three to four times that of PRAL, for physical activity two to seven times, and for fat mass (per standard deviation) around nine times that of PRAL.

Within this cohort, a difference of 10 years in age in the multivariate model was associated with a 1.15 kg lower FFM. Compared with this the difference of 0.28 kg per quartile of PRAL was equivalent to 24.3 % i.e. around a

Table 2 Characteristics of the participants and intakes of nutrients and foods according to quartile of Potential Renal Acid Load (PRAL) intake of 2,689 women aged 18–79 years

	Q1		Q2		Q3		Q4		<i>P</i> ^a
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
PRAL, mEq/day	-24.44	8.43	-12.10	2.11	-5.23	1.98	4.83	6.14	–
Characteristics									
Age, years	50.2	11.7	48.5	12.1	48.5	12.4	45.7	14.1	<0.001
Height, cm	162.4	6.0	162.4	5.9	162.3	6.0	162.6	6.2	0.58
Weight, kg	65.7	11.1	65.6	11.3	65.6	11.6	65.5	11.1	0.74
BMI, kg/m ²	24.9	4.0	24.9	4.1	24.9	4.4	24.8	4.2	0.75
Fat mass, kg	22.7	7.7	22.6	8.0	23.1	8.3	22.7	7.7	0.75
Current smokers, % (N)	17.7 (119)		18.6 (125)		17.8 (120)		19.4 (130)		0.85
Physical activity, % active (N)	18.7 (126)		19.6 (132)		23.2 (156)		26.5 (178)		0.002
Nutrients									
Protein, g/day	77.9	20.5	76.4	20.5	80.7	20.4	89.2	22.4	<0.001
Phosphorus, mg/day	1553	415	1533	390	1536	405	1593	415	0.11
Calcium, mg/day	1163	386	1102	356	1119	375	1146	376	0.59
Potassium, mg/day	4587	1030	3909	890	3750	892	3603	886	<0.001
Magnesium, mg/day	382	94.4	336	87.0	329	89.0	326	87.6	<0.001
Foods									
Meat, g/day	72	41	82	44	95	44	124	57	<0.001
Fish, g/day	33	24	33	26	36	25	39	28	<0.001
Eggs, g/day	10.0	10.1	9.7	9.8	10.7	10.6	11.3	10.4	0.007
Cereals, g/day	247	112	250	106	265	111	297	121	<0.001
Dairy, g/day	432	207	415	196	433	200	421	206	0.67
Fruit and vegetables, g/day	796	361	564	238	498	213	420	191	<0.001

Values are mean, SD

^a *P* for trend across quartiles calculated using linear regression

quarter of the effect of the difference in age. For FFM% and FFMI the equivalent figures were 19.5 and 52.9 % indicating that the scale of the effect of PRAL in relation to a decade of age was between 20 and 53 %.

The proportion of fruits and vegetables to the total amount of meat, fish, dairy, eggs and cereal foods (FNVEG:PROTCER) ranged from 0.3 to 1.4 Q1 vs Q4, Fig 1. The ratio of FNVEG:PROTCER was positively and significantly associated with FFM, FFM% and FFMI (all *P*<0.025) and there were differences of 1.05 kg for FFM between Q1 and Q4, of 0.67 % for FFM% and 0.32 kg/m² for FFMI.

Discussion

In this study of 18–79 year old women, we found a significant positive association between measures of lean body mass and a more alkaline dietary load. Differences of 0.79 kg for FFM, 1.06 % for FFM% and 0.24 kg/m² for FFMI were found between the most alkaline and most acidic diets, equating to differences that were between 1.6 and

2.0 % of the mean indexes for this population. These associations were significant after adjustment for age, physical activity, misreporting and smoking habit and for fat mass (for FFM, FFMI), with only slight attenuation of findings after adjustment for percentage protein intake. They did not differ according to menopausal status. The differences we found were over and above the known effects of age and other covariates and equated to a scale of effect that was between 20 and 53 % of the scale of the observed association with 10 years of age. We also observed a significant positive association with a greater proportion of fruit and vegetables to fish, meat, eggs, dairy and cereal foods (acidogenic to alkaligenic foods) with a ratio of 1.4 being optimum. To our knowledge, this is the first study to investigate associations between dietary acid–base load and estimates of skeletal muscle mass in a range of young to older-aged women.

Our findings were observed across all age ranges and there was not only a difference between those with the most acidogenic (positive PRAL intake) and alkaligenic diet but there was also a continuous association with better

Table 3 Indexes of muscle mass according to quartile of PRAL intake in 2689 women aged 18–79 years before and after adjustment for age, physical activity, smoking habit and fat mass and also for percentage protein intake, values are mean (SEM) unless SD also provided

	Model	Q1		Q2		Q3		Q4		Diff ^a	P ^b
		Mean	SEM (SD)								
Fat-free mass (FFM), kg	1	39.82	0.20 (5.42)	39.67	0.14 (5.29)	39.52	0.14 (5.22)	39.37	0.19 (5.38)	-1.1	0.13
	2	40.10	0.20	39.73	0.19	39.27	0.19	39.31	0.20	-2.0	0.001
	3	40.02	0.20	39.70	0.19	39.28	0.19	39.38	0.21	-1.6	0.010
Percentage fat-free mass (FFM%)	1	61.25	0.23 (6.41)	61.09	0.17 (6.52)	60.94	0.17 (6.73)	60.78	0.23 (6.36)	-0.8	0.18
	2	61.47	0.25	61.34	0.25	60.82	0.26	60.41	0.25	-1.7	<0.001
	3	61.35	0.24	61.31	0.25	60.85	0.26	60.54	0.25	-1.3	0.008
Fat-free mass Index (FFMI), kg/m ²	1	15.10	0.06 (1.70)	15.03	0.04 (1.69)	14.97	0.05 (1.74)	14.90	0.06 (1.78)	-1.3	0.040
	2	15.14	0.06	15.05	0.06	14.90	0.06	14.90	0.07	-1.6	0.002
	3	15.16	0.06	15.05	0.06	14.90	0.06	14.88	0.06	-1.9	0.001

Values are mean, SEM

^a Diff difference between quartiles 1 and 4 as a percentage of the mean of the population $((Q4-Q1)/\text{mean of the population}) \times 100$. *Model 1* unadjusted association. *Model 2* adjusted for age, physical activity, dietary misreporting and smoking habit (for FFM%). FFMI and FFM were also adjusted for fat mass. *Model 3* includes the same variables as model 2 with the addition of percentage protein (protein as percentage of energy)

^b P for trend across quartiles calculated using linear regression

indexes of muscle mass across the range of the more alkaline diet (negative PRAL intake) in this population. Our findings were also observed within a population with relatively high levels of physical activity, were not related to zygosity and also within-pair analyses were not informative.

We chose to investigate not only FFM and FFM% but also the FFMI as indexes of muscle mass because fat-free mass increases with both increased height and weight. The FFMI is considered to be a preferable method for comparison purposes since it uses the square of the height as the denominator, effectively eliminating the differences associated with greater height [32].

Comparison of indexes of muscle mass with other studies

The results of our study are comparable with estimates of muscle mass from other studies. In American Caucasian women from the NHANES III study, the mean FFMI (calculated using skin fold measures) was 17.9 kg/m² in women aged 40–99 years [32, 41] however, body weight and BMI were greater in this population compared to our cohort. In a US population study using DXA measures of body composition, mean fat-free mass was 43.9 kg in non-Hispanic white women [42]. In a European study of women in Switzerland, the mean FFMI (measured using bioelectrical impedance) was 15.6 in 18–24-year old women and 16.7 in 55–64 year old women [32]. The mean FFM and FFMI in our study was relatively lower than in these studies; however, the other populations were either younger, heavier or taller than our cohort or the data mainly obtained via impedance methods, which may not be directly comparable with our DXA values.

Our data also showed age-related differences in muscle mass which are comparable with other studies although other studies used bioimpedance as well as DXA methods [41–43]. Estimates from other studies in women ranged from differences of lean mass of 1.5 kg per decade in sedentary women 45 years and over to a decline in fat-free mass index of 0.17 kg/m², over 5 years, in women aged 75 years and over [41–44].

Intervention studies with potassium salts

Although the relationship between the extreme metabolic acidosis of chronic renal failure and muscle loss has been well established there have been comparatively few studies investigating the effects of dietary acid load on muscle mass in healthy people and to our knowledge there have been none in a population including a wide age range [11, 27]. Two intervention studies designed to understand the effect of reducing the metabolic acidosis of chronic renal disease, using sodium bicarbonate as the source of bicarbonate, found improvements in nitrogen balance, in serum albumin and in mid-arm muscle circumference after supplementation for 2 years (greater nitrogen excretion occurs during muscle breakdown) [45, 46]. Two supplementation studies of potassium bicarbonate in healthy post-menopausal women or in older men and women found significant improvements in nitrogen excretion, with the more recent study suggesting this effect might be mediated by IGF-1 [24, 25]. Furthermore, a cross-sectional study of potassium excretion in older people found a significant positive association with percentage lean body mass, and change in lean

Table 4 The association of indexes of muscle mass with potential renal acid load in 2689 women aged 18 to 79 years

	β^a	95 % CI	<i>P</i>	<i>R</i> ²
Fat-free mass (per kg)				
Model 2				
PRAL (per quartile)	-0.28	-0.45,-0.12	0.001	0.25
Age (per 10 years)	-1.15	-1.33,-0.97	<0.001	
Current smoking (yes versus no)	-0.76	-1.23,-0.29	0.001	
EI:EER (per SD)	-0.35	-0.54,-0.15	0.001	
Physical activity (active versus inactive)	0.84	0.37, 1.30	<0.001	
Fat mass (per SD)	2.53	2.27, 2.79	<0.001	
Model 3				
PRAL (per quartile)	-0.23	-0.41,-0.06	0.010	0.25
Age (per 10 years)	-1.12	-1.30,-0.94	<0.001	
Current smoking (yes versus no)	-0.69	-1.16,-0.22	0.004	
EI:EER (per SD)	-0.40	-0.61,-0.20	<0.001	
Physical activity (active versus inactive)	0.81	0.34, 1.27	0.001	
Fat mass (per SD)	2.53	2.27, 2.80	<0.001	
Percentage protein intake (per quartile)	-0.16	-0.36, 0.03	0.090	
Percentage fat-free mass (per %)				
Model 2				
PRAL (per quartile)	-0.37	-0.57,-0.17	<0.001	0.15
Age (per 10 years)	-1.90	-2.11,-1.68	<0.001	
Current smoking (yes versus no)	-1.29	-1.90,-0.68	<0.001	
EI:EER (per SD)	0.79	0.54, 1.05	<0.001	
Physical activity (active versus inactive)	2.49	1.90, 3.07	<0.001	
Model 3				
PRAL (per quartile)	-0.29	-0.51,-0.08	0.008	0.16
Age (per 10 years)	-1.85	-2.07,-1.63	<0.001	
Current smoking (yes versus no)	-1.24	-1.86,-0.63	<0.001	
EI:EER (per SD)	0.70	0.40, 0.97	<0.001	
Physical activity (active versus inactive)	2.43	1.85, 3.01	<0.001	
Percentage protein intake (per quartile)	-0.26	-0.50,-0.02	0.031	
Fat-free mass index (per kg/m ²)				
Model 2				
PRAL (per quartile)	-0.09	-0.14,-0.03	0.002	0.22
Age (per 10 years)	-0.17	-0.23,-0.11	<0.001	
Current smoking (yes versus no)	-0.28	-0.43,-0.13	<0.001	
EI:EER (per SD)	-0.08	-0.15,-0.015	0.017	
Physical activity (active versus inactive)	0.17	0.01, 0.32	0.042	
Fat mass (per SD)	0.82	0.74, 0.91	<0.001	
Model 3				
PRAL (per quartile)	-0.10	-0.16,-0.04	0.001	0.22
Age (per 10 years)	-0.18	-0.24,-0.12	<0.001	
Current smoking (yes versus no)	-0.29	-0.44,-0.14	<0.001	
EI:EER (per SD)	-0.07	-0.14, 0.00	0.60	
Physical activity (active versus inactive)	0.17	0.01, 0.33	0.032	
Fat mass (per SD)	0.82	0.73, 0.91	<0.001	
Percentage protein intake (per quartile)	0.05	-0.01, 0.11	0.14	

^aThe beta coefficients represent the difference in the indexes of fat-free mass according to the variable specified: per quartile of PRAL (potential renal acid load), age per 10 years, smoking (yes vs no), energy intake to estimated energy expenditure ratio – EI:EER divided by its standard deviation, physical activity (active vs inactive), fat mass in kg divided by its standard deviation (7.93), percentage protein intake (per quartile)

body mass over a 3-year period, of around 0.65 % lean body mass per standard deviation of potassium excretion,

equivalent to around 0.48 kg of lean body mass in that population [26].

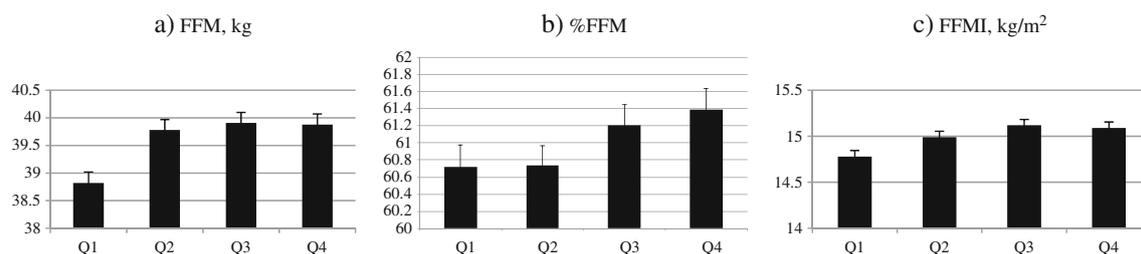


Fig. 1 Indexes of skeletal muscle mass according to quartiles of the proportion of fruit and vegetables to the total amount of meat, fish, dairy foods, eggs, and cereal foods (FNVEG:PROTCER). All analyses adjusted for age, physical activity, smoking habit and misreporting

using ANCOVA. Quartile values for ratio of fruit and vegetables to total meat, fish, eggs, dairy foods and cereal foods—mean, (SD) Q1 0.33(0.09) Q2 0.54(0.06) Q3 0.77(0.08) Q4 1.35(0.57). **a** P for trend $P=0.001$, **b** P for trend $P=0.025$, **c** P for trend $P=0.001$

Significance of the findings

We estimated that the mean acid–base load of the diet in this study was -9.24 mEq/day. This compared with other estimates in UK women of -7.2 mEq/day, indicates that the diet was on average more alkaline than in other studies although our range was large ≈ 29.27 mEq/day [17, 21, 23]. Protein and adequate nitrogen balance is essential for maintenance of muscle mass [3, 14–16]. However, our findings remained significant after accounting for the protein content of the diet suggesting that although protein is important for maintenance of muscle mass (the average intake was 81.1 g per day, 16.6 % of energy) other nutrients in the diet associated with more alkalinogenic foods, particularly potassium and magnesium, may also be relevant. Indeed the proportion of fruits and vegetables to foods with a potential acidogenic profile (meats, fish, eggs, dairy, cereals) was positively and significantly associated with indexes of skeletal muscle mass. The results of the hypotheses from our study suggest that the optimal diet for maintenance of muscle mass should contain not only protein but also other nutrients associated with the alkalinogenic foods fruits and vegetables. In our study, we found the optimal ratio of alkalinogenic to acidogenic foods: fruits and vegetables compared with intakes of meats, fish, eggs, dairy, and cereals to be 1.4.

Strengths and weaknesses of this study

The strengths of this study include the large sample size, the wide age range of our participants and the objective assessment of body composition by DXA. We also utilised the wide age range to determine whether associations were greater in pre than post-menopausal women. Limitations of our study warrant discussion. As with any cross-sectional study design, no causal associations can

be made and we cannot exclude the possibility of residual confounding, although we adjusted for possible confounders. However, given our detailed adjustment for potential confounders it is unlikely that these would account for the observed results. We relied on an FFQ for our dietary measures, although in a validation study estimates of PRAL from this FFQ and from a 7-day diary showed associations of a similar scale with pH measured in 24-h urine excretion, indicating that for PRAL the FFQ estimates as efficiently as a diary [17]. More specifically, comparison of the beta coefficients of the association with 24-h urine pH were -0.13 ($P=0.001$) per standard deviation of PRAL for the FFQ and -0.16 ($P=0.001$) for the diary [17]. Our findings relate to women, and further studies are required to examine if similar associations are observed in male participants.

Conclusion

In conclusion, we found a small significant positive association between a more alkaline diet and indexes of skeletal muscle mass indicating a potential role for diet in prevention of muscle loss. The association was independent of age, physical activity, potential misreporting and protein intake, and equated to a scale of effect that was between one fifth and one half of the scale of observed relationship with 10 years of age. Since conservation of muscle mass is vital for health and may have a role in prevention of fractures, the results point towards potential targeted interventions, particularly in the pre-frail elderly, where preventing muscle loss is a priority for optimal health.

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Conflicts of interest None.

References

- Wolfe RR (2006) The underappreciated role of muscle in health and disease. *Am J Clin Nutr* 84(3):475–482
- Beenakker KG, Ling CH, Meskers CG, de Craen AJ, Stijnen T, Westendorp RG, Maier AB (2010) Patterns of muscle strength loss with age in the general population and patients with a chronic inflammatory state. *Ageing Res Rev* 9(4):431–436. doi:10.1016/j.arr.2010.05.005
- Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, Deutz NE, Doehner W, Fearon KC, Ferrucci L, Hellerstein MK, Kalantar-Zadeh K, Lochs H, MacDonald N, Mulligan K, Muscaritoli M, Ponikowski P, Posthauer ME, Rossi Fanelli F, Schambelan M, Schols AM, Schuster MW, Anker SD (2010) Nutritional recommendations for the management of sarcopenia. *J Am Med Dir Assoc* 11(6):391–396. doi:10.1016/j.jamda.2010.04.014
- Harvey N, Dennison E, Cooper C (2010) Osteoporosis: impact on health and economics. *Nat Rev Rheumatol* 6(2):99–105. doi:10.1038/nrrheum.2009.260
- Foundation IO (2010) Facts and statistics about osteoporosis and its impact. <http://www.iofbonehealth.org/facts-and-statistics.html>. Accessed 14/01/11 2010
- Bogal LH, Latvala A, Kaprio J, Sovijarvi O, Rissanen A, Pietilainen KH An investigation into the relationship between soft tissue body composition and bone mineral density in a young adult twin sample. *J Bone Miner Res* 26 (1):79–87. doi:10.1002/jbmr.192
- MacInnis RJ, Cassar C, Nowson CA, Paton LM, Flicker L, Hopper JL, Larkins RG, Wark JD (2003) Determinants of bone density in 30- to 65-year-old women: a co-twin study. *J Bone Miner Res* 18 (9):1650–1656. doi:10.1359/jbmr.2003.18.9.1650
- Salamone LM, Glynn N, Black D, Epstein RS, Palermo L, Meilahn E, Kuller LH, Cauley JA (1995) Body composition and bone mineral density in premenopausal and early perimenopausal women. *J Bone Miner Res* 10(11):1762–1768. doi:10.1002/jbmr.5650101120
- Arden NK, Spector TD (1997) Genetic influences on muscle strength, lean body mass, and bone mineral density: a twin study. *J Bone Miner Res* 12(12):2076–2081. doi:10.1359/jbmr.1997.12.12.2076
- Rolland Y, Lauwers-Cances V, Cristini C, Abellan van Kan G, Janssen I, Morley JE, Vellas B (2009) Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPI-Demiologie de l'Osteoporose) Study. *Am J Clin Nutr* 89(6):1895–1900. doi:10.3945/ajcn.2008.26950
- Mitch WE (1996) Metabolic acidosis stimulates protein metabolism in uremia. *Miner Electrolyte Metab* 22(1–3):62–65
- Workeneh BT, Rondon-Berrios H, Zhang L, Hu Z, Ayehu G, Ferrando A, Koppale JD, Wang H, Storer T, Fournier M, Lee SW, Du J, Mitch WE (2006) Development of a diagnostic method for detecting increased muscle protein degradation in patients with catabolic conditions. *J Am Soc Nephrol* 17(11):3233–3239. doi:10.1681/ASN.2006020131
- Scott D, Blizzard L, Fell J, Ding C, Winzenberg T, Jones G (2010) A prospective study of the associations between 25-hydroxy-vitamin D, sarcopenia progression and physical activity in older adults. *Clin Endocrinol (Oxf)* 73(5):581–587. doi:10.1111/j.1365-2265.2010.03858.x
- Wackerhage H, Rennie MJ (2006) How nutrition and exercise maintain the human musculoskeletal mass. *J Anat* 208(4):451–458. doi:10.1111/j.1469-7580.2006.00544.x
- Paddon-Jones D, Short KR, Campbell WW, Volpi E, Wolfe RR (2008) Role of dietary protein in the sarcopenia of aging. *Am J Clin Nutr* 87(5):1562S–1566S. doi:87/5/1562S [pii]
- Meng X, Zhu K, Devine A, Kerr DA, Binns CW, Prince RL (2009) A 5-year cohort study of the effects of high protein intake on lean mass and BMC in elderly postmenopausal women. *J Bone Miner Res* 24(11):1827–1834. doi:10.1359/jbmr.090513
- Welch AA, Mulligan A, Bingham SA, Khaw KT (2008) Urine pH is an indicator of dietary acid–base load, fruit and vegetables and meat intakes: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk population study. *Br J Nutr* 99(6):1335–1343. doi:10.1017/S0007114507862350
- Remer T, Manz F (1995) Potential renal acid load of foods and its influence on urine pH. *J Am Diet Assoc* 95(7):791–797. doi:10.1016/S0002-8223(95)00219-7
- Frassetto LA, Todd KM, Morris RC Jr, Sebastian A (1998) Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr* 68 (3):576–583
- Alexy U, Remer T, Manz F, Neu CM, Schoenau E (2005) Long-term protein intake and dietary potential renal acid load are associated with bone modeling and remodeling at the proximal radius in healthy children. *Am J Clin Nutr* 82(5):1107–1114
- Macdonald HM, New SA, Fraser WD, Campbell MK, Reid DM (2005) Low dietary potassium intakes and high dietary estimates of net endogenous acid production are associated with low bone mineral density in premenopausal women and increased markers of bone resorption in postmenopausal women. *Am J Clin Nutr* 81 (4):923–933
- New SA, MacDonald HM, Campbell MK, Martin JC, Garton MJ, Robins SP, Reid DM (2004) Lower estimates of net endogenous non-carbonic acid production are positively associated with indexes of bone health in premenopausal and perimenopausal women. *Am J Clin Nutr* 79(1):131–138
- Welch AA, Bingham SA, Reeve J, Khaw KT (2007) More acidic dietary acid–base load is associated with reduced calcaneal broadband ultrasound attenuation in women but not in men: results from the EPIC-Norfolk cohort study. *Am J Clin Nutr* 85(4):1134–1141
- Ceglia L, Harris SS, Abrams SA, Rasmussen HM, Dallal GE, Dawson-Hughes B (2009) Potassium bicarbonate attenuates the urinary nitrogen excretion that accompanies an increase in dietary protein and may promote calcium absorption. *J Clin Endocrinol Metab* 94(2):645–653. doi:10.1210/jc.2008-1796
- Frassetto L, Morris RC Jr, Sebastian A (1997) Potassium bicarbonate reduces urinary nitrogen excretion in postmenopausal women. *J Clin Endocrinol Metab* 82(1):254–259
- Dawson-Hughes B, Harris SS, Ceglia L (2008) Alkaline diets favor lean tissue mass in older adults. *Am J Clin Nutr* 87 (3):662–665
- Workeneh BT, Mitch WE (2010) Review of muscle wasting associated with chronic kidney disease. *Am J Clin Nutr* 91(4):1128S–1132S. doi:10.3945/ajcn.2010.28608B
- Cassidy A, Skidmore P, Rimm EB, Welch A, Fairweather-Tait S, Skinner J, Burling K, Richards JB, Spector TD, MacGregor AJ (2009) Plasma adiponectin concentrations are associated with body composition and plant-based dietary factors in female twins. *J Nutr* 139(2):353–358. doi:10.3945/jn.108.098681
- Andrew T, Hart DJ, Snieder H, de Lange M, Spector TD, MacGregor AJ (2001) Are twins and singletons comparable? A study of disease-related and lifestyle characteristics in adult women. *Twin Res* 4(6):464–477
- Teucher B, Skinner J, Skidmore PM, Cassidy A, Fairweather-Tait SJ, Hooper L, Roe MA, Foxall R, Oyston SL, Cherkas LF, Perks

- UC, Spector TD, MacGregor AJ (2007) Dietary patterns and heritability of food choice in a UK female twin cohort. *Twin Res Hum Genet* 10(5):734–748. doi:[10.1375/twin.10.5.734](https://doi.org/10.1375/twin.10.5.734)
31. Samaras K, Kelly PJ, Chiano MN, Spector TD, Campbell LV (1999) Genetic and environmental influences on total-body and central abdominal fat: the effect of physical activity in female twins. *Ann Intern Med* 130(11):873–882
32. Kyle UG, Schutz Y, Dupertuis YM, Pichard C (2003) Body composition interpretation. Contributions of the fat-free mass index and the body fat mass index. *Nutrition* 19(7–8):597–604
33. Welch AA, Luben R, Khaw KT, Bingham SA (2005) The CAFE computer program for nutritional analysis of the EPIC-Norfolk food frequency questionnaire and identification of extreme nutrient values. *J Hum Nutr Diet* 18(2):99–116. doi:[10.1111/j.1365-277X.2005.00593.x](https://doi.org/10.1111/j.1365-277X.2005.00593.x)
34. Agency FS (2002) McCance and Widdowson's the composition of foods sixth summary edition. Royal Society of Chemistry, Cambridge
35. Otten JJ, Hellwig JP, Meyers LD (2006) DRI, dietary reference intakes: the essential guide to nutrient requirements. National Academies Press, Washington, D.C
36. Rennie KL, Coward A, Jebb SA (2007) Estimating under-reporting of energy intake in dietary surveys using an individualised method. *Br J Nutr* 97(6):1169–1176. doi:[10.1017/S0007114507433086](https://doi.org/10.1017/S0007114507433086)
37. Paddon-Jones D, Sheffield-Moore M, Cree MG, Hewlings SJ, Aarsland A, Wolfe RR, Ferrando AA (2006) Atrophy and impaired muscle protein synthesis during prolonged inactivity and stress. *J Clin Endocrinol Metab* 91(12):4836–4841. doi:[10.1210/jc.2006-0651](https://doi.org/10.1210/jc.2006-0651)
38. Szulc P, Duboeuf F, Marchand F, Delmas PD (2004) Hormonal and lifestyle determinants of appendicular skeletal muscle mass in men: the MINOS study. *Am J Clin Nutr* 80(2):496–503
39. Castillo EM, Goodman-Gruen D, Kritiz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor E (2003) Sarcopenia in elderly men and women: the Rancho Bernardo study. *Am J Prev Med* 25(3):226–231
40. Petersen AM, Magkos F, Atherton P, Selby A, Smith K, Rennie MJ, Pedersen BK, Mittendorfer B (2007) Smoking impairs muscle protein synthesis and increases the expression of myostatin and MAFbx in muscle. *Am J Physiol Endocrinol Metab* 293(3):E843–848. doi:[10.1152/ajpendo.00301.2007](https://doi.org/10.1152/ajpendo.00301.2007)
41. Obisesan TO, Aliyu MH, Bond V, Adams RG, Akomolafe A, Rotimi CN (2005) Ethnic and age-related fat free mass loss in older Americans: the Third National Health and Nutrition Examination Survey (NHANES III). *BMC Publ Health* 5:41. doi:[10.1186/1471-2458-5-41](https://doi.org/10.1186/1471-2458-5-41)
42. Li C, Ford ES, Zhao G, Balluz LS, Giles WH (2009) Estimates of body composition with dual-energy X-ray absorptiometry in adults. *Am J Clin Nutr* 90(6):1457–1465. doi:[10.3945/ajcn.2009.28141](https://doi.org/10.3945/ajcn.2009.28141)
43. Dey DK, Bosaeus I, Lissner L, Steen B (2009) Changes in body composition and its relation to muscle strength in 75-year-old men and women: a 5-year prospective follow-up study of the NORA cohort in Goteborg, Sweden. *Nutrition* 25(6):613–619. doi:[10.1016/j.nut.2008.11.023](https://doi.org/10.1016/j.nut.2008.11.023)
44. Kyle UG, Melzer K, Kayser B, Picard-Kossovsky M, Gremion G, Pichard C (2006) Eight-year longitudinal changes in body composition in healthy Swiss adults. *J Am Coll Nutr* 25(6):493–501
45. Papadoyannakis NJ, Stefanidis CJ, McGeown M (1984) The effect of the correction of metabolic acidosis on nitrogen and potassium balance of patients with chronic renal failure. *Am J Clin Nutr* 40(3):623–627
46. de Brito-Ashurst I, Varaganam M, Raftery MJ, Yaqoob MM (2009) Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 20(9):2075–2084. doi:[10.1681/ASN.2008111205](https://doi.org/10.1681/ASN.2008111205)