Dietary Phosphorus and Ambulatory Blood Pressure in African Americans: The Jackson Heart Study

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BACKGROUND

Higher dietary phosphorus is associated with left ventricular hypertrophy and mortality, which are blood pressure (BP)-related outcomes. For this reason, we hypothesized that dietary phosphorus may be associated with adverse clinic and ambulatory BP patterns.

METHODS

Our study included 973 African American adults enrolled in the Jackson Heart Study (2000–2004) with 24-hour ambulatory BP monitoring (ABPM) data at baseline. We quantified dietary phosphorus from a validated Food Frequency Questionnaire as follows: (i) absolute daily intake, (ii) ratio of phosphorus-to-protein intake, (iii) phosphorus density, and (iv) energy-adjusted phosphorus intake. Using multivariable linear regression, we determined associations between dietary phosphorus intake and systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure in clinic and over daytime, nighttime, and 24-hour periods from ABPM. Extent of nocturnal BP dipping was also assessed. Using logistic regression, we modeled relationships between dietary phosphorus intake and clinically relevant qualitative BP phenotypes, such as masked, sustained, or white-coat hypertension and normotension.

RESULTS

There were no statistically significant associations between phosphorus intake and SBP or pulse pressure in adjusted models. Most metrics of higher phosphorus intake were associated with lower daytime, nighttime, and clinic DBP. Higher phosphorus intake was not associated with clinic or ABPM-defined hypertension overall, but most metrics of higher phosphorus intake were associated with lower odds of sustained hypertension compared to sustained normotension, white-coat hypertension, and masked hypertension. There were no associations between dietary phosphorus and nocturnal BP dipping.

CONCLUSIONS

These data do not support a role for higher phosphorus intake and higher BP in African Americans.

Keywords: African American; ambulatory blood pressure; blood pressure; chronic kidney disease; diet; hypertension; nutrition; phosphorus.

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Hypertension is an increasingly common health condition that disproportionately affects African Americans.¹ The prevention of high blood pressure (BP) can substantially lower global cardiovascular disease, making risk factor studies a high impact area.² Recent expert working groups have highlighted opportunities to study risk factors for hypertension

in African Americans using the rich data available through the Jackson Heart Study (JHS), a population-based cohort of African Americans in the greater Jackson, Mississippi area.³ In addition to other questions, determining the association between nutrients and BP was identified as an important research opportunity.³ In this study, we evaluated the role of

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excess dietary phosphorus as a risk factor for hypertension and abnormal clinic and ambulatory BP patterns in African Americans using data from the JHS.

Excess dietary phosphorus is a growing public health concern due to overall increases in dietary phosphorus intake at the population level⁴ and well-described links between deranged phosphorus homeostasis and adverse cardiovascular outcomes.^{5–7} Specifically, high intake of phosphorus, particularly from highly absorbable sources such as phosphorus-based food additives, may lead to abnormalities in the phosphorus axis, including high concentrations of serum phosphorus and the phosphorus regulatory hormone fibroblast growth factor 23.^{8–11} In animal models, phosphorus loading has been shown to increase BP and promote endothelial dysfunction.^{12,13} Short-term physiologic studies in humans also support a role of phosphorus loading in altered vascular function,¹³ and some observational studies suggest that high dietary phosphorus intake may associate with adverse outcomes, such as left ventricular hypertrophy and mortality.^{14,15} Due to the strong association of BP with these outcomes, we hypothesized that high dietary phosphorus intake may contribute to higher BP levels.

METHODS

Study population

We conducted a cross-sectional study using data from the JHS at baseline. Between 2000 and 2004, the JHS enrolled 5,306 African Americans, aged 20–95 years, from the Jackson, Mississippi Tri-County area. Our study focused on 973 participants with adequate measures of dietary intake and a complete 24-hour ambulatory blood pressure monitoring (ABPM) recording at the baseline visit.¹⁶ The JHS was approved by institutional review boards at the University of Mississippi Medical Center, Jackson State University, and Tougaloo College. All participants provided written informed consent.

Data collection

Our primary exposure was dietary phosphorus, assessed from a regionally appropriate Food Frequency Questionnaire (FFQ).¹⁷ Primary outcomes were mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP), mean pulse pressure defined as the difference between mean SBP and mean DBP, and BP phenotypes determined from clinic BP measures and a 24-hour ABPM recording.¹⁶

Exposure measures

The JHS collected dietary intake using a shortened version of the Delta Nutrition Intervention Research Initiative FFQ, specifically designed to capture the typical diets and regional food consumption patterns of the Lower Mississippi Delta region. The Delta Nutrition Intervention Research Initiative FFQ has been validated against 24-hour recall interviews and nutrient biomarkers in the JHS.^{17,18} The short form of this FFQ querying 158 food items was used in the full JHS cohort. Participants with extreme energy intakes (≤ 600 or

$\geq 4,800$ kcal/day) were excluded.¹⁹ Total dietary phosphorus and other nutrients were derived from the Nutrition Data System for Research software developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, Minnesota. Phosphorus is common in dairy and meat products, but it is also present in increasing quantities as a food additive.^{4,20} To better isolate variation in nonprotein phosphorus, we calculated the ratio of phosphorus-to-protein intake as an additional metric. To account for the correlation between phosphorus and energy intake, we evaluated phosphorus density, as the ratio of phosphorus-to-total energy, and energy-adjusted phosphorus intake, as the residual from the linear regression of phosphorus on total energy added to the phosphorus intake value at the mean energy intake.²¹

Outcome measures

Clinic BP was measured 2 times 1-minute apart using a random-zero sphygmomanometer calibrated to a semiautomatic oscillometric device, as described previously.²² The two BP measurements were averaged for analysis. Overall, 1,148 JHS participants underwent 24-hour ABPM using a commercial device (SpaceLabs 90207) on the nondominant arm, with BP recorded every 20 minutes.¹⁶ Data were evaluated for quality and a complete ABPM recording was defined using the International Database on Ambulatory Blood Pressure in relation to Cardiovascular Outcomes (IDACO) criteria. Specifically, participants were required to have ≥ 10 daytime (10 AM to 8 PM) and ≥ 5 nighttime (midnight to 6 AM) SBP and DBP measurements to be included in this analysis.²³ Daytime and nighttime periods exclude sleep and wake transitions.²⁴ All BP measurements from the ABPM were used to determine 24-hour SBP, DBP, and pulse pressure.

Nocturnal BP dipping was calculated as the percent difference between mean daytime and nighttime SBP and classified as dipper ($\geq 10\%$) or nondipper ($< 10\%$).²⁵ We used hypertension definitions from the 2013 European Society of Hypertension classifications for qualitative BP phenotypes,²⁶ and defined clinic hypertension as clinic SBP ≥ 140 or DBP ≥ 90 mm Hg; 24-hour hypertension as mean 24-hour SBP ≥ 130 or DBP ≥ 80 mm Hg; and sustained hypertension as the presence of both clinic and 24-hour hypertension. White-coat hypertension was defined as clinic hypertension without 24-hour hypertension, and masked hypertension as the presence of 24-hour hypertension without clinic hypertension.²⁷

Covariates

We calculated estimated glomerular filtration rate (eGFR) using the CKD-EPI equation for serum creatinine.²⁸ Demographic features and medical history were obtained by self-report and physical examination. Diabetes mellitus was based on hemoglobin A1c $\geq 6.5\%$ or a fasting glucose ≥ 126 mg/dL, or use of hypoglycemic medications or insulin, or self-reported diabetes. Current cigarette smoking status and current alcohol consumption were determined by self-report on questionnaires. Use of antihypertensive medication classes within the previous 2 weeks was ascertained by

self-report and by review of pill bottles and prescriptions.²⁹ Classes of antihypertensive medications considered included β -blockers, calcium channel blockers, diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aldosterone antagonists, α -blockers, centrally acting agonists, and vasodilators.

Statistical analysis

We evaluated the association of each dietary phosphorus intake metric with mean SBP and DBP (daytime, nighttime, 24-hour, and clinic), pulse pressure (daytime, nighttime, and 24-hour), and percentage of nocturnal BP dipping using linear regression. Models were adjusted for age, sex, and income level, followed by additional adjustment for diabetes, current smoking status, current alcohol use, eGFR, number of antihypertensive medication classes, total energy intake, and dietary sodium consumption. In models of phosphorus density and energy-adjusted phosphorus, total energy was not included as a covariate because it was already incorporated in these metrics and because exploratory models revealed that results were not meaningfully changed with its inclusion.^{30,31} Because of the suspected collinearity with energy intake and scaled nutrients, primary models did not include adjustment for body mass index. Sensitivity analyses considered additional adjustment for body mass index.

We used logistic regression with aforementioned adjustments for associations between dietary phosphorus metrics and BP phenotypes. For sustained hypertension, the presence of the phenotype was compared to all other phenotypes (sustained normotension, white-coat hypertension, and masked hypertension) combined and among those with clinic-defined hypertension (sustained vs. white-coat hypertension). Due to the potential impact of kidney disease, diabetes, and antihypertensive medications on BP, we tested for interaction and fit models stratified by eGFR, diabetes, and the number of antihypertensive medication classes being taken. All statistical analyses were performed using RStudio version 0.99.484 (RStudio, Boston, MA) and data as released in the JHS 2016 Vanguard Center Data Package.

RESULTS

Study population and participant characteristics

Of total 5,306 JHS participants, 1,148 performed 24-hour ABPM.¹⁶ We excluded 74 participants without a complete 24-hour ABPM recording based on IDACO criteria, 99 participants without reliable dietary intake information,¹⁹ and 2 participants with a history of dialysis or kidney transplant. The study population had a mean ($\pm$ SD) age of 59.3 ± 10.8 years, and 69.3% of participants were female (Table 1).

Similar to typical dietary intake reported by the United States Department of Agriculture (www.ars.usda.gov), median dietary phosphorus intake in the study population was 1,056 mg/day (interquartile range [IQR]: 802–1,421 mg/day). Scaled to protein intake (phosphorus-to-protein ratio) and total energy intake (phosphorus density),

mean ($\pm$ SD) phosphorus intake was 15.6 ± 3.12 mg/g and 0.614 ± 0.144 mg/kcal, respectively. Median energy-adjusted phosphorus intake was 1,126 mg/day (IQR: 993–1,275 mg/day). Participants with higher absolute phosphorus intake were younger, less likely to be female, and more likely to consume alcohol (Table 1). Absolute dietary phosphorus was highly correlated with intake of total energy ($r = 0.83$), sodium ($r = 0.81$), protein ($r = 0.89$ overall; $r = 0.87$ for animal protein and $r = 0.72$ for vegetable protein), and potassium ($r = 0.81$). Meanwhile, intakes of calcium ($r = 0.57$), magnesium ($r = 0.72$), and folate ($r = 0.56$) were moderately correlated with dietary phosphorus possibly due to nondietary supplements contributing to these nutrients (Supplementary Figures 1 and 2).

Overall, 63.1% of participants had hypertension, 22.5% had diabetes, and 6.4% had an eGFR <60 ml/min/1.73 m². Mean ($\pm$ SD) clinic SBP and DBP were 127.1 ± 17.0 and 77.3 ± 10.1 mm Hg, respectively (Table 1). Median nocturnal BP dipping was 6.8% (IQR: 1.6–11.4%), and 66.6% of participants were nondippers ($n = 648$). Overall, 407 participants (41.8%) had 24-hour hypertension, 250 (25.8%) had clinic hypertension, 98 (10.1%) had sustained hypertension, 306 (31.6%) had masked hypertension, and 152 (15.7%) had white-coat hypertension. The prevalence of these abnormal BP phenotypes was similar across quartiles of dietary phosphorus (Supplementary Table 1).

Dietary phosphorus and blood pressure

There were no statistically significant associations between dietary phosphorus metrics and 24-hour SBP, DBP, or pulse pressure (Table 2). Results were similar in sensitivity analyses with adjustment for body mass index. In contrast to our expectation, higher phosphorus intake metrics were associated with lower daytime and nighttime DBP (Figure 1). Daytime DBP was 1.67 mm Hg lower per 500 mg/day higher absolute phosphorus intake ($P = 0.002$), 1.45 mm Hg lower per 0.2 mg/kcal higher phosphorus density ($P < 0.001$), and 1.69 mm Hg lower per 500 mg/day higher energy-adjusted phosphorus intake ($P = 0.001$). Also, nighttime DBP was 1.32 mm Hg lower per 500 mg/day higher absolute phosphorus intake ($P = 0.04$), 0.98 mm Hg lower per 0.2 mg/kcal higher phosphorus density ($P = 0.04$), and 1.26 mm Hg lower per 500 mg/day higher energy-adjusted phosphorus intake ($P = 0.04$; Figure 2). These associations did not persist when normalizing phosphorus intake to protein. There were no statistically significant relationships between dietary phosphorus and SBP or pulse pressure, daytime or nighttime (Figures 1 and 2).

There were no independent associations of dietary phosphorus metrics with clinic SBP. Higher dietary phosphorus was associated with lower clinic DBP using most metrics in fully adjusted models. Specifically, clinic DBP was 1.43 mm Hg lower per 500 mg/day higher absolute phosphorus intake ($P = 0.02$), 1.10 mm Hg lower per 5.0 mg/g higher phosphorus-to-protein ratio ($P = 0.05$), 0.81 mm Hg lower per 0.2 mg/kcal higher phosphorus density ($P = 0.09$), and 1.14 mm Hg lower per 500 mg/day higher energy-adjusted phosphorus intake ($P = 0.05$). For all SBP, DBP, and pulse

Table 1. Characteristics of participants by absolute dietary phosphorus intake (mg/day)

Characteristic	Overall (N = 973)	Q1 231–801 (n = 243)	Q2 802–1,055 (n = 243)	Q3 1,056–1,420 (n = 243)	Q4 1,421–3,769 (n = 244)
Age (years)	59.3 ± 10.8	61.6 ± 10.3	59.8 ± 10.8	58.7 ± 10.6	56.9 ± 10.9
Female	674 (69.3%)	198 (81.5%)	187 (77.0%)	151 (62.1%)	138 (56.6%)
Income					
Poor or lower-middle	326 (33.5%)	87 (35.8%)	76 (31.3%)	88 (36.2%)	75 (30.7%)
Upper-middle or affluent	532 (54.7%)	123 (50.6%)	139 (57.2%)	131 (53.9%)	139 (57.0%)
Missing data	115 (11.8%)	33 (13.6%)	28 (11.5%)	24 (9.9%)	30 (12.3%)
Current smoker	90 (9.2%)	21 (8.6%)	15 (6.2%)	26 (10.7%)	28 (11.5%)
Current alcohol use	418 (43.0%)	96 (39.5%)	98 (40.3%)	98 (40.3%)	126 (51.6%)
Daytime SBP (mm Hg)	129.3 ± 13.5	129.6 ± 13.5	129.4 ± 13.6	129.7 ± 12.7	128.5 ± 14.1
Daytime DBP (mm Hg)	77.8 ± 9.2	76.9 ± 9.8	77.8 ± 8.9	77.9 ± 8.6	78.8 ± 9.5
Daytime PP (mm Hg)	51.5 ± 11.2	52.7 ± 11.3	51.6 ± 11.7	51.9 ± 10.9	49.8 ± 10.7
Nighttime SBP (mm Hg)	121.0 ± 15.9	120.3 ± 15.7	121.5 ± 16.2	122.0 ± 16.2	120.1 ± 15.8
Nighttime DBP (mm Hg)	68.3 ± 10.3	66.7 ± 9.3	68.6 ± 10.3	68.7 ± 10.8	69.3 ± 10.3
Nighttime PP (mm Hg)	52.7 ± 11.6	53.6 ± 11.8	52.9 ± 12.1	53.2 ± 11.5	50.8 ± 10.8
Hypertension	614 (63.1%)	166 (68.3%)	145 (59.7%)	161 (66.3%)	142 (58.2%)
Number of anti-HTN classes	1.12 ± 1.17	1.23 ± 1.18	1.12 ± 1.17	1.14 ± 1.17	1.01 ± 1.14
Diabetes	238 (24.5%)	64 (26.3%)	59 (24.3%)	60 (24.7%)	55 (22.5%)
eGFR (ml/min/1.73 m ²)	91.4 ± 21.2	87.1 ± 20.9	93.0 ± 18.6	93.1 ± 21.2	92.3 ± 23.2
<60	62 (6.4%)	22 (9.1%)	9 (3.7%)	13 (5.3%)	18 (7.4%)
Albuminuria (mg/g) ^a	6.0 (4.0–12.0)	7.0 (4.0–12.0)	6.0 (4.0–10.6)	5.0 (4.0–12.0)	6.0 (4.0–12.0)
Dietary sodium (mg)	3,247 ± 1,358	1,930 ± 512	2,726 ± 617	3,532 ± 883	4,822 ± 1,203
Dietary protein (g)	75.7 ± 33.8	42.7 ± 10.9	61.4 ± 12.7	81.2 ± 18.1	118.1 ± 29.5
Animal protein	46.9 ± 27.6	22.1 ± 7.4	34.0 ± 10.3	51.1 ± 15.5	80.2 ± 27.3
Vegetable protein	21.2 ± 8.3	13.6 ± 3.9	19.0 ± 4.7	22.7 ± 6.1	29.5 ± 8.1
Total energy (kcal)	1,905 ± 751	1,133 ± 314	1,624 ± 364	2,088 ± 484	2,772 ± 572
Dietary folate (μg)	320.0 ± 135.7	223.9 ± 112.6	303.1 ± 107.1	324.2 ± 101.2	428.5 ± 134.1
Dietary calcium (mg)	843.0 ± 452.7	537.8 ± 342.4	769.2 ± 396.9	871.2 ± 371.8	1,192.4 ± 431.8
Dietary magnesium (mg)	295.1 ± 119.4	197.3 ± 82.4	260.9 ± 80.6	307.2 ± 76.5	414.3 ± 113.3
Dietary potassium (mg)	2,567 ± 1,001	1,631 ± 534	2,235 ± 565	2,723 ± 617	3,675 ± 885

Mean ± SD shown for continuous variables (unless otherwise indicated), number of participants (proportion) shown for categorical variables. Abbreviations: DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HTN, hypertension; PP, pulse pressure; Q, quartile; SBP, systolic blood pressure.

^aMedian (25th percentile to 75th percentile).

pressure measures, there was no evidence of interaction of dietary phosphorus with eGFR, diabetes, or number of antihypertensive medication classes (*P* interaction > 0.05 for each). Selected results stratified by antihypertensive medication use (none vs. 1 or more classes) are presented in [Supplementary Table 2](#). Results were similar if participants with hypertension at baseline were excluded.

Dietary phosphorus and qualitative BP phenotypes

There were no statistically significant associations between any dietary phosphorus metrics and nocturnal BP dipping

or odds of nondipping in adjusted models ([Table 3](#)). Higher absolute dietary phosphorus was associated with lower odds of clinic hypertension in univariate and demographic-adjusted analyses ([Table 3](#)), but this did not persist after full adjustment. No other associations were present between phosphorus intake and clinic hypertension. There were no associations between phosphorus intake and 24-hour hypertension. Higher dietary phosphorus was associated with reduced odds of sustained hypertension compared to all other phenotypes: odds ratio (OR) 0.56 (95% confidence interval [CI]: 0.33–0.91) per 500 mg/day higher absolute phosphorus intake; OR 0.64 (95% CI: 0.43–0.95) per

Table 2. Association between dietary phosphorus intake and 24-hour blood pressure (mm Hg)

	Unadjusted		Adjusted for demographics ^a		Fully adjusted ^b	
	Difference	P	Difference	P	Difference	P
24-hour systolic BP						
Per +500 mg/day phosphorus	−0.10	0.83	+0.01	0.98	−0.61	0.50
Per +5.0 mg/g phosphorus-to-protein ratio	−0.25	0.73	−0.48	0.52	−0.66	0.42
Per +0.2 mg/kcal phosphorus density	−0.22	0.72	−0.37	0.55	−0.49	0.49
Per +500 mg/day energy-adjusted phosphorus	−0.32	0.69	−0.51	0.53	−0.55	0.52
24-hour diastolic BP						
Per +500 mg/day phosphorus	+0.24	0.42	+0.01	0.97	−0.48	0.41
Per +5.0 mg/g phosphorus-to-protein ratio	−1.11	0.02	−0.85	0.08	−0.92	0.09
Per +0.2 mg/kcal phosphorus density	−0.43	0.28	−0.30	0.47	−0.30	0.51
Per +500 mg/day energy-adjusted phosphorus	−0.50	0.34	−0.40	0.45	−0.41	0.46
24-hour pulse pressure						
Per +500 mg/day phosphorus	−0.33	0.35	−0.003	0.99	−0.13	0.85
Per +5.0 mg/g phosphorus-to-protein ratio	+0.86	0.14	+0.37	0.52	+0.26	0.69
Per +0.2 mg/kcal phosphorus density	+0.21	0.67	−0.08	0.88	−0.19	0.73
Per +500 mg/day energy-adjusted phosphorus	+0.18	0.78	−0.11	0.86	−0.14	0.84

Abbreviation: BP, blood pressure.

^aModels were adjusted for age, sex, and income level.

^bModels were adjusted for age, sex, income level, diabetes, smoking status, current alcohol use, estimated glomerular filtration rate, number of antihypertensive medication classes, total energy intake, and dietary sodium. In models incorporating energy into the exposure (phosphorus density and energy-adjusted phosphorus intake), total energy was not added as a covariate. In models using phosphorus density as the exposure, we adjusted for sodium density (dietary sodium to total energy).

5.0 mg/g higher phosphorus-to-protein ratio; OR 0.73 (95% CI: 0.51–1.04) per 0.2 mg/kcal higher phosphorus density; and OR 0.59 (95% CI: 0.37–0.93) per 500 mg/day higher energy-adjusted phosphorus intake (Table 3). Because the reference group includes multiple phenotypes, including lower- and higher-risk groups, we further divided this analysis into subsets defined by high clinic BP (sustained vs. white-coat hypertension) and 24-hour hypertension (sustained vs. masked hypertension). There was a lower odds of sustained hypertension vs. masked hypertension with some dietary phosphorus metrics. However, there were no associations between dietary phosphorus and odds of sustained hypertension vs. white-coat hypertension for any metric (Supplementary Table 3). There were no statistically significant interactions between dietary phosphorus and eGFR, diabetes, or the number of antihypertensive medication classes for any hypertension phenotype.

DISCUSSION

We sought to determine the association between dietary phosphorus intake and BP in African Americans. Although prior studies have evaluated the potential role of phosphorus in BP regulation, few studies have investigated this specifically among African Americans or used ABPM which more precisely characterizes 24-hour BP and qualitative BP phenotypes.^{31–33} This inquiry is highly relevant in light of the high risk of hypertension among African Americans,

growing use of phosphorus-based food additives, and myriad reported associations between phosphorus homeostasis, left ventricular hypertrophy, and cardiovascular disease.^{3–7} Overall, we did not find consistent statistically significant associations between dietary phosphorus intake and BP level or phenotype using any metric of phosphorus intake, including total phosphorus intake, phosphorus-to-protein ratio, phosphorus density, or energy-adjusted phosphorus. By some metrics of phosphorus intake, higher intake was associated with lower daytime and nighttime DBP, but not with 24-hour DBP or pulse pressure. Discrepancies between daytime and nighttime DBP and 24-hour DBP outcomes are likely related to the inclusion of highly variable transition periods in the mornings and evenings in 24-hour measurements.²⁴ However, SBP correlates more strongly with cardiovascular outcomes and thus the relevance of our lower DBP finding is unclear.^{34,35} Finally, higher phosphorus intake was also associated with reduced odds of sustained hypertension when compared to all other phenotypes, which is a mixture of both higher- and lower-risk phenotypes, such as masked hypertension, white-coat hypertension, and normotension. Evaluating just those with clinic hypertension, a similar association was not observed for sustained hypertension compared to the lower-risk phenotype of white-coat hypertension. For this reason and due to many phenotypes tested, we recommend interpreting this finding cautiously.

We hypothesized that increased dietary phosphorus would be associated with higher BP levels based on the high

Figure 1. Association of dietary phosphorus intake with daytime ambulatory blood pressure ($N = 973$). Dietary phosphorus was expressed as absolute intake, normalized to protein intake, and energy-adjusted phosphorus intake, and shown are their relationships with (a) daytime systolic blood pressure, (b) daytime diastolic blood pressure, and (c) daytime pulse pressure. Effect sizes are in mm Hg, with 95% confidence intervals shown. Models were adjusted for age, sex, income level, diabetes, smoking status, current alcohol use, estimated glomerular filtration rate, number of antihypertensive medication classes, total energy intake, and dietary sodium. In models incorporating energy into the exposure (phosphorus density and energy-adjusted phosphorus intake), total energy intake was not added as a covariate. In models using phosphorus density as the exposure, we adjusted for sodium density (dietary sodium to total energy).

risk of left ventricular hypertrophy, heart failure, and cardiovascular disease associated with higher serum phosphorus or its regulatory hormones.^{6,7,36,37} Animal and human studies suggest that phosphorus loading may directly affect vascular compliance, calcification, and vasodilation as a plausible mechanism directly promoting hypertension.^{13,38–40} Recently, the phosphorus regulatory hormone, fibroblast growth factor 23, was reported to increase the absorption of sodium in the distal tubule of the kidney as another potential mechanism.⁴¹ Nonetheless, we did not find associations between high dietary phosphorus intake and BP using clinic or ABPM measures. Prior studies have reported associations

between higher dietary phosphorus and *lower* BP in the United States and internationally.^{31,32,42} However, all of these studies are limited by the strong correlations between dietary phosphorus and other BP-lowering nutrients, such as calcium, magnesium, potassium, and whole grains.^{31,32} In fact, the major sources of phosphorus in these prior studies were fish and dairy products, 2 food groups widely thought to improve BP.⁴³ In the Atherosclerosis Risk in Communities Study, the beneficial association between dietary phosphorus intake and BP was only evident for dairy-based phosphorus.³² Nationally representative estimates suggest that grains, including refined grains, are the largest source of

Figure 2. Association of dietary phosphorus intake with nighttime ambulatory blood pressure. Dietary phosphorus was expressed as absolute intake, normalized to protein intake, normalized to total energy intake, and energy-adjusted phosphorus intake, and shown are their relationships with (a) nighttime systolic blood pressure, (b) nighttime diastolic blood pressure, and (c) nighttime pulse pressure. Effect sizes are given in mm Hg, with 95% confidence intervals shown. Models were adjusted for age, sex, income level, diabetes, smoking status, current alcohol use, estimated glomerular filtration rate, number of antihypertensive medication classes, total energy intake, and dietary sodium. In models incorporating energy into the exposure (phosphorus density and energy-adjusted phosphorus intake), total energy intake was not added as a covariate. In models using phosphorus density as the exposure, we adjusted for sodium density (dietary sodium to total energy).

dietary phosphorus intake;⁴ therefore, the relevance of these prior results to current American consumption and across different sources of dietary phosphorus remains unknown. Different dietary sources of phosphorus, such as unprocessed vs. processed meat and dairy, whole vs. refined grains and phosphorus-containing beverages, are each absorbed differently in the gastrointestinal tract, a feature that we were unable to account for fully in this analysis.^{44,45} In this study, we attempted to isolate the impact of inorganic phosphorus food additives from healthier unprocessed sources by calculating the phosphorus-to-protein ratio, but results were largely unchanged. This method may not be able to

fully account for additives as many legumes have high phosphorus-to-protein ratios despite being unprocessed. A more direct method of accounting for phosphorus-based food additives or examining absorbable phosphorus may yield different results.

In addition to the earlier consideration, our study is among the first to evaluate the association between dietary phosphorus and BP in African Americans. Total dietary phosphorus intake is lower in African Americans according to many studies where it may associate with lower levels of dairy and protein intake.^{4,32} Different patterns of phosphorus sources in African Americans may be responsible for

Table 3. Association between dietary phosphorus intake and odds of abnormal BP phenotypes

	Unadjusted	Adjusted for demographics ^a	Fully adjusted ^b
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Nondipping nocturnal BP (N = 973; 648 cases)			
Per +500 mg/day phosphorus	1.11 (0.97–1.28)	1.15 (1.00–1.33)	1.05 (0.79–1.39)
Per +5.0 mg/g phosphorus-to-protein ratio	0.96 (0.78–1.20)	0.91 (0.73–1.14)	0.92 (0.72–1.19)
Per +0.2 mg/kcal phosphorus density	1.15 (0.95–1.40)	1.16 (0.95–1.41)	1.02 (0.82–1.27)
Per +500 mg/day energy-adjusted phosphorus	1.17 (0.92–1.50)	1.19 (0.93–1.53)	1.05 (0.80–1.37)
Clinic hypertension (N = 969; 250 cases)			
Per +500 mg/day phosphorus	0.85 (0.73–0.98)	0.85 (0.72–0.99)	0.78 (0.56–1.07)
Per +5.0 mg/g phosphorus-to-protein ratio	0.95 (0.75–1.20)	0.89 (0.69–1.12)	0.79 (0.60–1.04)
Per +0.2 mg/kcal phosphorus density	0.95 (0.78–1.16)	0.92 (0.75–1.13)	0.92 (0.72–1.15)
Per +500 mg/day energy-adjusted phosphorus	0.85 (0.65–1.11)	0.81 (0.61–1.06)	0.77 (0.56–1.04)
24-hour hypertension (N = 973; 407 cases)			
Per +500 mg/day phosphorus	0.98 (0.86–1.11)	0.99 (0.87–1.13)	0.85 (0.65–1.10)
Per +5.0 mg/g phosphorus-to-protein ratio	0.98 (0.80–1.21)	0.97 (0.79–1.20)	0.96 (0.75–1.21)
Per +0.2 mg/kcal phosphorus density	0.96 (0.80–1.14)	0.95 (0.79–1.14)	0.91 (0.75–1.12)
Per +500 mg/day energy-adjusted phosphorus	0.91 (0.72–1.14)	0.90 (0.71–1.13)	0.85 (0.66–1.09)
Sustained hypertension (N = 969; 98 cases)			
Per +500 mg/day phosphorus	0.76 (0.59–0.95)	0.77 (0.60–0.98)	0.56 (0.33–0.91)
Per +5.0 mg/g phosphorus-to-protein ratio	0.81 (0.57–1.15)	0.73 (0.51–1.04)	0.64 (0.43–0.95)
Per +0.2 mg/kcal phosphorus density	0.81 (0.59–1.10)	0.77 (0.56–1.05)	0.73 (0.51–1.04)
Per +500 mg/day energy-adjusted phosphorus	0.67 (0.44–1.00)	0.61 (0.39–0.93)	0.59 (0.37–0.93)

Abbreviations: BP, blood pressure; CI, confidence interval; OR, odds ratio.

^aModels were adjusted for age, sex, and income level.

^bModels were adjusted for age, sex, income level, diabetes, smoking status, current alcohol use, estimated glomerular filtration rate, number of antihypertensive medication classes, total energy intake, and dietary sodium. In models incorporating energy into the exposure (phosphorus density and energy-adjusted phosphorus intake), total energy was not added as a covariate. In models using phosphorus density as the exposure, we adjusted for sodium density (dietary sodium to total energy).

conflicting results between this and prior studies. In fact, in the Atherosclerosis Risk in Communities Study, there was no association between dietary phosphorus intake and incident hypertension among the African American subgroup.³² These disparate findings across groups may suggest that it is dietary patterns and not phosphorus per se that drove the associations with favorable BP.

Our study has some important limitations. First, quantifying dietary phosphorus intake is challenging given incomplete labeling of phosphorus content in many processed foods and reporting biases common to FFQs.⁴⁶ Additionally, our methodology did not fully account for the differences in animal, plant, and inorganic sources of phosphorus and may not be able to fully adjust for and remove collinearity with other nutrients.⁴⁷ Another limitation is the relatively small proportion of JHS participants (22%) who underwent ABPM. Although all individuals were invited to participate after completing their baseline visit, there could be unknown confounders associated with ambulatory BP patterns that influenced a participant's decision to undergo or decline ABPM. Finally, our study was cross-sectional in nature and

additional ABPM measurements were not available over follow-up. Our study also had many strengths including the use of a regionally tailored and validated FFQ, gold standard BP measurement methodology, and an adequate sample size.

In summary, higher dietary phosphorus intake was not consistently associated with higher prevalence of hypertension or more adverse BP phenotypes among African Americans. Our findings could imply that the association between disturbed phosphorus homeostasis and cardiovascular disease is mediated by pathways other than BP. However, given the limitations of dietary phosphorus assessment with incomplete accounting of different sources of phosphorus intake, additional studies capturing the complexity of phosphorus content and sources are needed.

SUPPLEMENTARY DATA

Supplementary data are available at *American Journal of Hypertension* online.

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

- Heidenreich PA, Trogon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khera A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PW, Woo YJ; American Heart Association Advocacy Coordinating Committee; Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Cardiovascular Nursing; Council on the Kidney in Cardiovascular Disease; Council on Cardiovascular Surgery and Anesthesia, and Interdisciplinary Council on Quality of Care and Outcomes Research. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation* 2011; 123:933–944.
- Sacco RL, Roth GA, Reddy KS, Arnett DK, Bonita R, Gaziano TA, Heidenreich PA, Huffman MD, Mayosi BM, Mendis S, Murray CJ, Perel P, Piñeiro DJ, Smith SC Jr, Taubert KA, Wood DA, Zhao D, Zoghbi WA. The heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modeling study from the American Heart Association and World Heart Federation. *Circulation* 2016; 133:e674–e690.
- Muntner P, Abdalla M, Correa A, Griswold M, Hall JE, Jones DW, Mensah GA, Sims M, Shimbo D, Spruill TM, Tucker KL, Appel LJ. Hypertension in blacks: unanswered questions and future directions for the JHS (Jackson Heart Study). *Hypertension* 2017; 69:761–769.
- McClure ST, Chang AR, Selvin E, Rebholz CM, Appel LJ. Dietary sources of phosphorus among adults in the United States: results from NHANES 2001–2014. *Nutrients* 2017;9:95.
- Scialla JJ, Wolf M. Roles of phosphate and fibroblast growth factor 23 in cardiovascular disease. *Nat Rev Nephrol* 2014; 10:268–278.
- Dhingra R, Sullivan LM, Fox CS, Wang TJ, D'Agostino RB Sr, Gaziano JM, Vasan RS. Relations of serum phosphorus and calcium levels to the incidence of cardiovascular disease in the community. *Arch Intern Med* 2007; 167:879–885.
- Lutsey PL, Alonso A, Selvin E, Pankow JS, Michos ED, Agarwal SK, Loehr LR, Eckfeldt JH, Coresh J. Fibroblast growth factor-23 and incident coronary heart disease, heart failure, and cardiovascular mortality: the Atherosclerosis Risk in Communities study. *J Am Heart Assoc* 2014; 3:e000936.
- Antoniucci DM, Yamashita T, Portale AA. Dietary phosphorus regulates serum fibroblast growth factor-23 concentrations in healthy men. *J Clin Endocrinol Metab* 2006; 91:3144–3149.
- Ferrari SL, Bonjour JB, Rizzoli R. Fibroblast growth factor-23 relationship to dietary phosphate and renal phosphate handling in healthy young men. *J Clin Endocrinol Metab* 2005; 90:1519–1524.
- Moore LW, Nolte JV, Gaber AO, Suki WN. Association of dietary phosphate and serum phosphorus concentration by levels of kidney function. *Am J Clin Nutr* 2015; 102:444–453.
- Burnett SM, Gunawardene SC, Brighurst FR, Juppner H, Lee H, Finkelstein JS. Regulation of C-terminal and intact FGF-23 by dietary phosphate in men and women. *J Bone Miner Res* 2006; 21:1187–1196.
- Bozic M, Panizo S, Sevilla MA, Riera M, Soler MJ, Pascual J, Lopez I, Freixenet M, Fernandez E, Valdivielso JM. High phosphate diet increases arterial blood pressure via a parathyroid hormone mediated increase of renin. *J Hypertens* 2014; 32:1822–1832.
- Shuto E, Taketani Y, Tanaka R, Harada N, Isshiki M, Sato M, Nashiki K, Amo K, Yamamoto H, Higashi Y, Nakaya Y, Takeda E. Dietary phosphorus acutely impairs endothelial function. *J Am Soc Nephrol* 2009; 20:1504–1512.
- Chang AR, Lazo M, Appel LJ, Gutiérrez OM, Grams ME. High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III. *Am J Clin Nutr* 2014; 99:320–327.
- Yamamoto KT, Robinson-Cohen C, de Oliveira MC, Kostina A, Nettleton JA, Ix JH, Nguyen H, Eng J, Lima JA, Siscovick DS, Weiss NS, Kestenbaum B. Dietary phosphorus is associated with greater left ventricular mass. *Kidney Int* 2013; 83:707–714.
- Booth JN III, Diaz KM, Seals SR, Sims M, Ravenell J, Muntner P, Shimbo D. Masked hypertension and cardiovascular disease events in a prospective cohort of blacks: the Jackson heart study. *Hypertension* 2016; 68:501–510.
- Carithers TC, Talegawkar SA, Rowser ML, Henry OR, Dubbert PM, Bogle ML, Taylor HA Jr, Tucker KL. Validity and calibration of food frequency questionnaires used with African-American adults in the Jackson Heart Study. *J Am Diet Assoc* 2009; 109:1184–1193.
- Talegawkar SA, Johnson EJ, Carithers TC, Taylor HA, Bogle ML, Tucker KL. Carotenoid intakes, assessed by food-frequency questionnaires (FFQs), are associated with serum carotenoid concentrations in the Jackson Heart Study: validation of the Jackson Heart Study Delta NRI Adult FFQs. *Public Health Nutr* 2008; 11:989–997.
- Djoussé L, Petrone AB, Blackshear C, Griswold M, Harman JL, Clark KR, Talegawkar S, Hickson DA, Gaziano JM, Dubbert PM, Correa A, Tucker KL, Taylor HA. Prevalence and changes over time of ideal cardiovascular health metrics among African-Americans: the Jackson Heart Study. *Prev Med* 2015; 74:111–116.
- Carrigan A, Klinger A, Choquette SS, Luzuriaga-McPherson A, Bell EK, Darnell B, Gutiérrez OM. Contribution of food additives to sodium and phosphorus content of diets rich in processed foods. *J Ren Nutr* 2014; 24:13–9, 19e1.
- Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr*. 1997;65(Suppl 4):1220S–1228S.
- Abdalla M, Booth JN III, Seals SR, Spruill TM, Viera AJ, Diaz KM, Sims M, Muntner P, Shimbo D. Masked hypertension and incident clinic hypertension among blacks in the Jackson Heart Study. *Hypertension* 2016; 68:220–226.
- Thijs L, Hansen TW, Kikuya M, Björklund-Bodegård K, Li Y, Dolan E, Tikhonoff V, Seidlerová J, Kuznetsova T, Stolarz K, Bianchi M, Richart T, Casiglia E, Malyutina S, Filipovsky J, Kawecka-Jaszcz K, Nikitin Y, Ohkubo T, Sandoya E, Wang J, Torp-Pedersen C, Lind L, Ibsen H, Imai Y, Staessen JA, O'Brien E; IDACO Investigators. The International Database of Ambulatory Blood Pressure in relation to Cardiovascular Outcome (IDACO): protocol and research perspectives. *Blood Press Monit* 2007; 12:255–262.
- Staessen JA, O'Brien ET, Amery AK, Atkins N, Baumgart P, De Cort P, Degaute JB, Dolenc P, De Gaudemaris R, Enström I. Ambulatory blood pressure in normotensive and hypertensive subjects: results from an international database. *J Hypertens Suppl* 1994; 12:S1–12.
- Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Guerrieri M, Gatteschi C, Zampi I, Santucci A, Santucci C, Reboldi

- G. Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. *Hypertension* 1994; 24:793–801.
26. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F; Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013; 31:1281–1357.
  27. O'Brien E, Parati G, Stergiou G. Ambulatory blood pressure measurement: what is the international consensus? *Hypertension* 2013; 62:988–994.
  28. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150:604–612.
  29. Harman J, Walker ER, Charbonneau V, Akylbekova EL, Nelson C, Wyatt SB. Treatment of hypertension among African Americans: the Jackson Heart Study. *J Clin Hypertens (Greenwich)* 2013; 15:367–374.
  30. Yoon CY, Park JT, Jhee JH, Noh J, Kee YK, Seo C, Lee M, Cha MU, Kim H, Park S, Yun HR, Jung SY, Han SH, Yoo TH, Kang SW. High dietary phosphorus density is a risk factor for incident chronic kidney disease development in diabetic subjects: a community-based prospective cohort study. *Am J Clin Nutr* 2017; 106:311–321.
  31. Elliott P, Kesteloot H, Appel LJ, Dyer AR, Ueshima H, Chan Q, Brown IJ, Zhao L, Stamler J; INTERMAP Cooperative Research Group. Dietary phosphorus and blood pressure: international study of macro- and micro-nutrients and blood pressure. *Hypertension* 2008; 51:669–675.
  32. Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, Kestenbaum BR, Chambless LE, Jacobs DR Jr. Dietary phosphorus, blood pressure, and incidence of hypertension in the atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. *Hypertension* 2010; 55:776–784.
  33. Joffres MR, Reed DM, Yano K. Relationship of magnesium intake and other dietary factors to blood pressure: the Honolulu heart study. *Am J Clin Nutr* 1987; 45:469–475.
  34. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT Jr, Narva AS, Ortiz E. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014; 311:507–520.
  35. McEvoy JW, Chen Y, Rawlings A, Hoogeveen RC, Ballantyne CM, Blumenthal RS, Coresh J, Selvin E. Diastolic blood pressure, subclinical myocardial damage, and cardiac events: implications for blood pressure control. *J Am Coll Cardiol* 2016; 68:1713–1722.
  36. Faul C, Amaral AP, Oskoue B, Hu MC, Sloan A, Isakova T, Gutiérrez OM, Aguilón-Prada R, Lincoln J, Hare JM, Mundel P, Morales A, Scialla J, Fischer M, Soliman EZ, Chen J, Go AS, Rosas SE, Nessel L, Townsend RR, Feldman HI, St John Sutton M, Ojo A, Gadegbeku C, Di Marco GS, Reuter S, Kentrup D, Tiemann K, Brand M, Hill JA, Moe OW, Kuro-O M, Kusek JW, Keane MG, Wolf M. FGF23 induces left ventricular hypertrophy. *J Clin Invest* 2011; 121:4393–4408.
  37. Scialla JJ, Xie H, Rahman M, Anderson AH, Isakova T, Ojo A, Zhang X, Nessel L, Hamano T, Grunwald JE, Raj DS, Yang W, He J, Lash JP, Go AS, Kusek JW, Feldman H, Wolf M; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. Fibroblast growth factor-23 and cardiovascular events in CKD. *J Am Soc Nephrol* 2014; 25:349–360.
  38. Scialla JJ, Lau WL, Reilly MP, Isakova T, Yang HY, Crouthamel MH, Chavkin NW, Rahman M, Wahl P, Amaral AP, Hamano T, Master SR, Nessel L, Chai B, Xie D, Kallem RR, Chen J, Lash JP, Kusek JW, Budoff MJ, Giachelli CM, Wolf M; Chronic Renal Insufficiency Cohort Study Investigators. Fibroblast growth factor 23 is not associated with and does not induce arterial calcification. *Kidney Int* 2013; 83:1159–1168.
  39. Jono S, McKee MD, Murry CE, Shioi A, Nishizawa Y, Mori K, Morii H, Giachelli CM. Phosphate regulation of vascular smooth muscle cell calcification. *Circ Res* 2000; 87:E10–E17.
  40. Adeney KL, Siscovick DS, Ix JH, Seliger SL, Shlipak MG, Jenny NS, Kestenbaum BR. Association of serum phosphate with vascular and valvular calcification in moderate CKD. *J Am Soc Nephrol* 2009; 20:381–387.
  41. Andrukhova O, Slavic S, Smorodchenko A, Zeitz U, Shalhoub V, Lanske B, Pohl EE, Erben RG. FGF23 regulates renal sodium handling and blood pressure. *EMBO Mol Med* 2014; 6:744–759.
  42. Tzoulaki I, Patel CJ, Okamura T, Chan Q, Brown IJ, Miura K, Ueshima H, Zhao L, Van Horn L, Daviglus ML, Stamler J, Butte AJ, Ioannidis JP, Elliott P. A nutrient-wide association study on blood pressure. *Circulation* 2012; 126:2456–2464.
  43. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997; 336:1117–1124.
  44. Karp H, Ekholm P, Kemi V, Hirvonen T, Lamberg-Allardt C. Differences among total and *in vitro* digestible phosphorus content of meat and milk products. *J Ren Nutr* 2012; 22:344–349.
  45. Karp H, Ekholm P, Kemi V, Itkonen S, Hirvonen T, Närkki S, Lamberg-Allardt C. Differences among total and *in vitro* digestible phosphorus content of plant foods and beverages. *J Ren Nutr* 2012; 22:416–422.
  46. Sarathy S, Sullivan C, Leon JB, Sehgal AR. Fast food, phosphorus-containing additives, and the renal diet. *J Ren Nutr* 2008; 18:466–470.
  47. St-Jules DE, Jagannathan R, Gutekunst L, Kalantar-Zadeh K, Sevvick MA. Examining the proportion of dietary phosphorus from plants, animals, and food additives excreted in urine. *J Ren Nutr* 2017; 27:78–83.