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Markers of Mineral Metabolism Are Not Associated With Aortic Pulse Wave Velocity in Community-Living Elderly Persons: The Health Aging and Body Composition Study

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Abstract

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BACKGROUND—Disorders in mineral metabolism are associated with risk for cardiovascular disease (CVD) events in patients with kidney disease as well as in the general population. This risk is thought to be mediated, in part, through the mechanism of stiffening of the arteries.

METHODS—The objective of this study was to evaluate the relationships between serum calcium, phosphorus, intact parathyroid hormone (iPTH), and 25-hydroxyvitamin D levels and arterial pulse wave velocity (aPWV) among 2,229 community-dwelling elderly persons participating in the Health Aging and Body Composition (Health ABC) study.

RESULTS—The mean age of the participants was 72 years; 52% were woman, 39% were black, and 17% had chronic kidney disease (CKD) (estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2). In parallel unadjusted analyses, the following associations were observed: 2.86% greater aPWV per 12 ng/ml (s.d.) lower 25-hydroxyvitamin D (95% confidence interval −4.38%, −1.31%), 3.04% greater aPWV per 28 pg/ml (s.d.) higher iPTH (95% confidence interval 1.42–4.68%), and 2.37% lower aPWV per 0.5 mg/dl (s.d.) higher phosphorus (95% confidence interval −3.90% to − 0.81%). Except for phosphorus, these associations were attenuated and rendered no longer statistically significant after adjustment for demographic risk factors, clinical site, season, medications and other CVD risk factors. The results were similar in men and women and were not dependent on the presence of CKD.

CONCLUSIONS—Among well-functioning community-dwelling elderly persons, only serum phosphorus was associated with aPWV; and this association was in the opposite direction of the one hypothesized. Factors other than vascular stiffening may mediate the relationship between disordered mineral metabolism and CVD events in community-living elders.

Keywords

arterial stiffness; blood pressure; cardiovascular disease; hypertension; kidney disease; mineral metabolism; PWV

Disorders of mineral metabolism are associated with a greater risk for cardiovascular (CVD) events in patients with kidney failure.[1–3] Recent studies demonstrate that this link may exist in the general population as well,[4–6] even in individuals with ostensibly normal kidney function. Specifically, higher serum intact parathyroid hormone (iPTH) and phosphorus levels and lower 25-hydroxyvitamin D levels are associated with incidence[4–7] and recurrence[8] of CVD events, CVD mortality,[5,6,9] and peripheral arterial disease[10] in community-living populations, independent of kidney function and traditional CVD risk factors. Although the mechanisms responsible are unknown, it is possible that disordered mineral metabolism may contribute to arterial calcium deposition and associated arterial stiffening. Therefore arterial stiffening may be in the causal pathway between altered mineral metabolism and CVD events. Several studies have shown that abnormalities in mineral metabolism are associated with arterial calcification in community-living populations,[7,10–12] but the relationship with arterial stiffening remains largely untested.

There are no studies to our knowledge that evaluate the relationships between serum mineral metabolism markers and arterial pulse wave velocity (aPWV) in community-living populations. Increasingly, aPWV has been used as a clinical gold-standard measure of large-artery stiffness. This measure is associated with CVD risk factors and independently associated with incidence rates of CVD events and CVD mortality in community-living elderly persons.[13] In order to investigate the potential mechanisms linking abnormalities in mineral metabolism with CVD events, we evaluated the associations between mineral metabolism markers (serum 25-hydroxyvitamin D, iPTH, phosphorus, and calcium) and aPWV in a community-living population of well-functioning elderly persons who were part of the Health Aging and Body Composition (Health ABC) study. We hypothesized that

higher serum phosphorus and iPTH and lower 25-hydroxyvitamin D would be associated with greater aPWV, independent of kidney function and traditional CVD risk factors.

METHODS

Study sample

The Health ABC study was designed to evaluate the impact of changes in weight and body composition on age-related physiologic and functional changes. Details of the study design have been described elsewhere.[14] Briefly, individuals of 70–79 years of age were recruited from Medicare eligibility lists from March 1997 through July 1998 at two field centers (Pittsburgh, PA and Memphis, TN). White participants were recruited from a random sample of the Medicare eligibility lists; black participants were recruited from all age-eligible individuals residing in the respective communities. The participants made a day-long visit to the clinic, during which baseline data were recorded, including medical history, the results of physical examination, and aPWV measurement. Eligibility for the study included the requirement that the participants had no difficulty in walking ¼ mile, climbing 10 steps, and performing the basic activities of daily living.

Data relating to aPWV were not available for 354 (12%) participants because of equipment problems. Another 233 (8%) participants had waveforms that were unusable for analysis for various reasons. Among the 2,488 participants with adequate aPWV measurements, 2,269 (91%) returned for the follow-up visit 1 year after baseline. At this time point, after an overnight fast, venous blood specimens were collected for analysis of serum phosphorus, calcium, iPTH, and 25-hydroxyvitamin D levels. All the participants gave their informed written consent, and the protocol was approved by the institutional review boards of the clinical sites and the Health ABC Coordinating Center.

Mineral metabolism markers

Blood specimens were stored at −70 °C at the Health ABC core laboratory (University of Vermont, Burlington, VT) until analysis in 2008. The measurement of 25-hydroxyvitamin D in serum samples was carried out using a two-step radioimmunoassay (25-hydroxyvitamin D 125I RIA Kit; DiaSorin, Stillwater, MN). The interassay coefficient of variation was 6.78% for log-transformed values. iPTH was measured in EDTA plasma, using a two-site immunoradiometric assay kit (N-tact PTHSP; DiaSorin). The interassay coefficient of variation for PTH was 8.6%. Total calcium was measured in serum samples with direct quantitative colorimetric determination using Stanbio Total Calcium LiquiColor Procedure No. 0500 (Stanbio Laboratory, Boerne, TX). The interassay coefficient of variation was 2.2%. Inorganic phosphorus was measured in serum samples with direct quantitative UV determination using Stanbio Phosphorus Liqui-UV Procedure No. 0830 (Stanbio Laboratory). The interassay coefficient of variation was 6.7%.

Aortic pulse wave velocity

The methods for measurement of aPWV in Health ABC have been described in detail.[13] In brief, aPWV was measured at the baseline study visit from simultaneous Doppler flow signals obtained from the right carotid and right femoral arteries, using nondirectional transcutaneous Doppler flow probes (model 810A, 9.0–10-MHz probes; Parks Medical Electronics, Aloha, OR). The distance between the carotid and femoral sampling sites was measured above the surface of the body with a metal tape measure. Digitized data were recorded by custom programming for subsequent analysis. Less compliant vessels are associated with a faster aPWV. Results from all acceptable runs were averaged for the final aPWV measure used in the analyses. Replicate measures of aPWV in 14 individuals revealed intraclass correlations of 0.88 between sonographers and 0.84 between readers.

Covariates

Covariates were measured at the baseline examination and included: (i) sociodemographic factors (age, gender, race, field center, and education level); (ii) lifestyle factors (smoking (current, former, never) alcohol use (>1 drink/day vs. less)); (iii) body mass index (kg/m^2); and (iv) comorbid medical conditions such as diabetes (use of hypoglycemic agents, self-report, fasting plasma glucose >126 mg/dl, or an oral glucose tolerance test >200 mg/dl), hypertension (use of antihypertensive medications, systolic blood pressure >140 mm Hg, or diastolic blood pressure >90 mm Hg), heart failure, CVD (CHD, myocardial infarction, angina, coronary artery bypass), peripheral arterial disease, and cerebrovascular disease. Cystatin C was measured in plasma specimens that had been stored at 70 °C at the Health ABC core laboratory (University of Vermont), by means of a BNII Nephelometer (Dade Behring, Deerfield, IL), incorporating a particle-enhanced immunonepholometric assay (N Latex Cystatin C).[15] For cystatin C, the intra-assay coefficient variations ranged between 2.0 and 2.8%, and interassay coefficient variations ranged between 2.3 and 3.1%. Estimated glomerular filtration rate ($eGFR_{cys}$) was calculated from the cystatin C value using the formula $eGFR_{cys} = 76.7 \times \text{cystatin C}^{-1.19}$ (ref. 16). Plasma glucose levels were measured by means of an automated glucose oxidase reaction (YSI2300 glucose analyzer; Yellow Springs Instruments, Yellow Springs, OH). High-density lipoprotein cholesterol and triglyceride concentrations were measured using a Vitros 950 analyzer (Johnson & Johnson, New Brunswick, NJ).

Statistical analyses

We categorized participants by quartiles of aPWV, and compared the distribution of demographics and covariates across quartiles using χ^2-test for categorical variables and analysis of variance or the Kruskal–Wallis tests for continuous variables, as appropriate. A Spearman correlation matrix was created to evaluate the correlations among phosphorus, calcium, iPTH, and 25-hydroxyvtamin D levels. Subsequently, linear regression was used to evaluate the associations between each of the mineral metabolism measures and aPWV. The value of aPWV was right-skewed, and therefore the data were log-transformed to approximate a Gaussian distribution. The results were subsequently back-transformed to provide adjusted geometric mean values of aPWV by mineral metabolism categories for the purposes of data presentation and greater interpretability. For each mineral metabolism measurement, the results were expressed on a continuous scale, modeled with standard deviation greater in each mineral metabolism measure to facilitate comparisons, and also as categorical predictors, using clinically relevant cutoff points. Sequential models were developed. Model 1 was unadjusted. Model 2 was adjusted for age, gender, race, clinical site, and season. The latter two covariates were included because of the known seasonal and geographic variations in 25-hydroxyvitamin D levels due to differences in exposure to sunlight, which may in turn influence iPTH, calcium, and phosphorus levels. Model 3 was adjusted for model 2 variables plus eGFR, body mass index, smoking, physical activity, diabetes, low-density lipoprotein, high-density lipoprotein, triglycerides, and lipid medication use. Model 4 included model 3 variables plus systolic blood pressure, diastolic blood pressure, and blood pressure medication use. These variables were added late in the sequence, because they may, in part, be markers of arterial stiffening, and therefore be related to the dependent variable. We evaluated two potential effect modifiers: (i) chronic kidney disease (CKD) and (ii) phosphorus levels. We defined CKD as an $eGFR_{cys}$ <60 ml/min/1.73 m^2, and a multiplicative interaction term (mineral metabolism measure × CKD (yes/no)) was evaluated within the final multivariable model. As regards phosphorus, in most prior population-based cohort studies, women have significantly higher phosphorus levels than men; in one earlier study, the association of phosphorus with CVD events was limited to men.[5] In another study, the association of serum phosphorus with greater left ventricular mass was also limited to men.[17] In this study, therefore, we evaluated a

multiplicative sex interaction term (mineral metabolism measures × female). *P* values <0.05 were considered statistically significant for all results including interaction terms. All the analyses were conducted in STATA version 10.0 (STATA, College Station, TX).

RESULTS

Of 2,488 Health ABC participants for whom aPWV measurements were available at baseline, 2,269 (91%) returned and provided blood specimens at the first annual follow-up visit. These individuals were included in this study. As compared to those included, those excluded because of missing blood specimens were more likely to be black. Other demographics and aPWV values were similar among included and excluded participants (Supplementary Table S1).

For the 2,269 participants retained in the study, the mean age was 74 ± 3 years; 52% were women, 39 % were black, 22% had diabetes, and 17 % had moderate CKD. The mean (s.d.) eGFR was 72 ± 16 ml/min/1.73 m^2, and the mean phosphorus, calcium, and 25-hydroxyvitamin D levels were 3.6 ± 0.5 mg/dl, 8.9 ± 0.4 mg/dl, and 26 ± 12 μg/l, respectively. The values of iPTH were right-skewed, with median (interquartile range) of 33.7 (25.2, 45.9) pg/ml. Similarly, aPWV was right-skewed with median value of 807 cm/s (interquartile range 642.7–1,052.5). The median values (interquartile range) were 825.5 (650.3, 1,068.5), 758.4 (599.5, 983.5), 868.0 (702.0, 1,118.5), and 809.5 (646.0, 1,079.0) in white men, white women, black men, and black women, respectively.

In comparison with individuals with lower aPWV, those with aPWV in the highest quartile were older, more likely to be male, and more likely to be black (Table 1). Individuals with higher aPWV had a higher prevalence of most of the traditional CVD risk factors, except for total and low-density lipoprotein cholesterol levels, which were similar across the quartiles. Participants in the highest aPWV quartile also had lower 25-hydroxyvitamin D and phosphorus concentrations and higher iPTH concentrations, whereas calcium concentrations were similar across aPWV quartiles. In unadjusted analyses, the four mineral metabolism measurements were moderately correlated with one another, with the strongest correlation being observed between iPTH and 25-hydroxyvitamin D (Spearman $r = -0.34$ $P \leq 0.0001$).

Serum 25-hydroxyvitamin D and aPWV

In unadjusted analysis, 25-hydroxyvitamin D and aPWV were inversely correlated. In unadjusted analysis, each s.d. (11.8 ng/dl) greater 25-hydroxyvitamin D level was associated with 2.8 % lower aPWV (Table 2). However, the magnitude of this association was attenuated by approximately one-third after adjustments were made for age, sex, race, field center, and season during which blood samples were obtained ($P = 0.04$). With additional adjustment for traditional CVD risk factors and kidney function, the association was further attenuated and rendered no longer statistically significant. Among these variables, body mass index was responsible for most of the attenuating effect. The results were similar in categorical analysis. As compared to participants with 25-hydroxyvitamin D levels >30 μg/l, those with levels <15 μg/l had 8% greater aPWV in unadjusted analysis; this association was markedly attenuated and no longer statistically significant in the final multivariable model (Table 3).

Intact PTH and aPWV

In unadjusted analysis, each standard deviation (27.7 pg/ml) greater iPTH was associated with a 3% greater aPWV (Table 2). The relationship persisted after adjusting for age, sex, race, field center, and season of blood measurement. However, the association was attenuated by ~50% with adjustment for traditional CVD risk factors and kidney function,

and rendered no longer statistically significant ($P = 0.09$). Among the covariates, eGFR provided the greatest attenuation. Further adjustment for systolic and diastolic blood pressure, and hypertension medication use abolished the remaining association. Similarly, in categorical analyses, iPTH >65 μg/l was associated with a 7% greater aPWV compared to individuals with lower iPTH levels, a relationship that was attenuated and no longer significant in the fully adjusted models (Table 3).

Serum phosphorus and aPWV

In unadjusted analysis, each standard deviation of higher in serum phosphorus (0.48 mg/dl) was associated with 2.4% lower aPWV (Table 2). The magnitude of this association was attenuated by ~25% after adjusting for age, sex, race, field location of center, and season of blood sampling. Further adjustment for traditional CVD risk factors (models 3 and 4) did not materially change this association, and therefore higher phosphorus remained significantly associated with lower aPWV in the final model ($P = 0.04$). When phosphorus was categorized, the results were generally similar, although the associations were not statistically significant in the fully adjusted models (Table 3).

Serum calcium and aPWV

We observed no significant association between calcium levels and aPWV in either unadjusted or adjusted models when evaluating calcium as a continuous predictor (Table 2). The results were similar in unadjusted models evaluating calcium categories. In the final model, individuals with serum calcium levels between 8.5 and 9.0 mg/dl had significantly lower aPWV values than individuals with lower calcium levels, but similar effects were not observed for calcium levels >9.0 mg/dl (Table 3).

Effect modification

We evaluated whether the effects of the associations between each of the mineral metabolism markers and aPWV were modified by CKD status or sex. We observed no evidence of effect modification (interaction P values all >0.05).

DISCUSSION

In the general population, mineral metabolism is associated with CVD events and arterial calcification.[7,10–12] However, the relationship between mineral metabolism and arterial stiffening is largely unknown. In this study, we provide a comprehensive evaluation of the relationships of mineral metabolism markers commonly measured in clinical practice and aortic pulse wave velocity, in a large sample of well-functioning community-living elderly persons. In unadjusted analysis, lower 25-hydroxyvitamin D, higher iPTH, and lower serum phosphorus was each associated with greater aPWV. However, in adjusted analysis serum phosphorus was the only mineral metabolism marker that was associated with aPWV independent of traditional CVD risk factors and kidney function, albeit in the opposite direction to that hypothesized.

Lower 25-hydroxyvitamin D levels have been associated with greater risk for CVD events and mortality.[7,18,19] Several hypotheses about the mechanisms that underlie this effect have been put forward; among them is the hypothesis that low levels of vitamin D may contribute to arterial calcification and stiffening. It is possible, however, that mechanisms other than arterial stiffening are responsible for the association between lower 25-hydroxyvitamin D levels and CVD events. It has been demonstrated that insufficiency of hydroxyvitamin D impacts CVD events through atherosclerosis,[11,20] cardiac hypertrophy,[21] and activation of the renin–angiotensin system.[22,23] In our study, although low 25-hydroxyvitamin D was associated with increased aPWV in unadjusted analyses, these results were attenuated and

no longer significant after adjustment for traditional CVD risk factors. Adjustment for body mass index, in particular, led to significant attenuation of the association. The association between 25-hydroxyvitamin D levels, obesity, insulin resistance, and diabetes is well established.[19,24,25] Therefore, our findings suggest that the association between low 25-hydroxyvitamin D and CVD events may, in part, reflect an association with metabolic risk factors and subclinical atherosclerosis rather than directly with arterial stiffening.

Higher phosphorus levels are also consistently associated with higher incidence of CVD,[4,5,11] recurrent CVD, and CVD-related mortality[8] in community-living populations. Prior studies have demonstrated that individuals with higher phosphorus levels are more likely to have stiffening of peripheral arteries.[12,26,27] One study suggested that this relationship is present only among persons with CKD.[26] Arterial calcification has been proposed as one of the mechanisms, given that phosphorus induces arterial calcification *in vitro*.[28] In our study, however, we observed that lower phosphorus levels were associated with greater aPWV, a finding which was the exact inverse of our initial hypothesis. Why is it that higher phosphorus levels are associated with stiffening of peripheral arteries (high ankle-brachial index) but not with higher aPWV? It is possible that these disparate findings may reflect regional anatomic differences in stiffness in the aorta vs. the ankle arteries. The anatomic character and mechanisms of arterial stiffening may differ according to the anatomical site. High ankle-brachial index has high specificity for a unique pattern of calcification limited to the arterial media (medial arterial calcification), which has the highest prevalence in the foot and ankle.[29] A high value of aPWV may more closely reflect increasing stiffness due to elastin breakdown and collagen deposition. Whether the presence of high aPWV values also reflects medial arterial calcification, atherosclerosis, advanced glycation end products, or a combination of these is unknown. Finally, it is possible that the relationship between phosphorus levels and aPWV is seen only at higher phosphorus levels such as those seen in patients undergoing dialysis, and that the association is missed in those with mild to moderate CKD.

Some studies have found an association between iPTH and mortality in the general population, independent of vitamin D levels and kidney function.[6,30,31] However, we observed no independent association between iPTH and aPWV. Our results would suggest that the mechanisms discussed earlier may play a more important role than arterial stiffening in community-living elders who are predominantly free of kidney disease.

Our study has several strengths. To our knowledge this is the first study to explore the relationship between mineral metabolism markers and aPWV, which is often considered as the gold-standard measurement of arterial stiffness. Health ABC provided a large representative sample of healthy, community-dwelling elderly persons, comprising those with CKD and without CKD. We were able to ascertain mineral metabolism comprehensively by studying four mineral metabolism markers and accounting for potential confounding variables. However, the study also had important limitations. First, measurements of mineral metabolism and aPWV were not concurrent (mineral measures were made ~1 year after aPWV) and temporal changes may have biased the results toward the null hypothesis. It is known that intraindividual variability is present in regard to mineral metabolism measurements.[32] To a smaller degree, the same may be true for aPWV measurements which are known to be affected by weight change.[33,34] Furthermore, because the Health ABC study was composed of well-functioning elderly persons, and given that those with kidney disease were primarily in stage 3 CKD (eGFR 30–60 ml/min/1.73 m^2), the associations between mineral metabolism markers and aPWV in younger populations, among elderly persons with functional disabilities, or in individuals with more advanced CKD remain unknown.

In conclusion, with the exception of serum phosphorus, we observed no independent associations between serum markers of mineral metabolism and aPWV in a relatively large, geographically diverse sample of well-functioning community-living elderly persons, predominantly free of kidney disease. Higher phosphorus levels were associated with lower aPWV values—an association in the opposite direction of the one hypothesized *a priori*. These results suggest that pathways other than aortic vascular stiffening may be important mediators of the relationship between abnormalities in mineral metabolism and adverse cardiovascular outcomes in community-living populations without severe kidney disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline characteristics by pulse wave velocity quartiles

aPWV (range (cm/sec))	**Q1 (<642.7)**	**Q2 (642.7–807)**	**Q3 (807–1,052.5)**	**Q4 (>1,052.5)**	***P* value**
n (%)	566 (25)	568 (25)	567 (25)	568 (25)	Total = 2,269
Age ± s.d., years	74 ± 3	74 ± 3	74 ± 3	74 ± 3	<0.001
Female, *n* (%)	326 (58)	313 (55)	280 (49)	264 (47)	<0.001
Black, *n* (%)	188 (33)	219 (39)	216 (38)	250 (44)	0.003
Smoking					
Current, *n* (%)	51 (9)	57 (10)	51 (9)	59 (10)	0.008
Former, *n* (%)	229 (41)	254 (45)	291 (51)	271 (48)	
Physical activity, METs[a]	648 (189, 1,488)	503 (86, 1,316)	470 (99, 1,305)	362 (34, 1,162)	<0.001
$eGFR_{cys}$ ± s.d. (ml/min/1.73 m^2)	82 ± 21	78 ± 20	77 ± 22	76 ± 20	<0.001
Total chol. ± s.d., mg/dl	203 ± 37	205 ± 38	204 ± 41	203 ± 40	0.81
HDL chol. ± s.d., mg/dl	57 ± 17	55 ± 17	53 ± 17	53 ± 18	<0.001
LDL chol. ± s.d., mg/dl	121 ± 32	123 ± 35	123 ± 36	122 ± 36	0.74
Lipid med use, *n* (%)	77 (14)	87 (15)	84 (15)	82 (15)	0.87
Diabetes, *n* (%)	73 (13)	108 (19)	142 (25)	178 (31)	<0.001
Hypertension, *n* (%)	284 (50)	345 (61)	372 (66)	415 (73)	<0.001
BMI ± s.d., kg/m^2	26.2 ± 4.4	27.6 ± 4.7	28.0 ± 4.9	27.6 ± 4.8	<0.001
Heart rate ± s.d., bpm	61.7 ± 10.0	64.6 ± 10.3	65.8 ± 11.7	66.9 ± 11.6	<0.001
SBP ± s.d., mm Hg	131 ± 19	134 ± 19	138 ± 21	142 ± 22	<0.001
DBP ± s.d., mm Hg	70 ± 11	72 ± 11	72 ± 12	73 ± 12	0.003
Diuretic use, *n* (%)	111 (20)	136 (24)	161 (28)	157 (28)	0.002
ACE inhibitor/ARB use, *n* (%)	82 (15)	86 (15)	100 (18)	122 (22)	0.007
β-Blocker use, *n* (%)	66 (12)	80 (14)	87 (15)	80 (14)	0.34
α-Blocker use, *n* (%)	17 (3)	18 (3)	29 (5)	34 (6)	0.03
Calcium-channel blocker use, *n* (%)	92 (16)	117 (21)	148 (26)	153 (27)	<0.001
Prevalent CVD, *n* (%)	129 (23)	133 (23)	177 (31)	166 (29)	0.002
25 (OH) vitamin D ± s.d., μg/l	27 ± 11	26 ± 12	26 ± 13	25 ± 11	0.001

aPWV (range (cm/sec))	Q1 (<642.7)	Q2 (642.7–807)	Q3 (807–1,052.5)	Q4 (>1,052.5)	*P* value
Intact PTH ± s.d., pg/ml[a]	31 (24, 43)	34 (25, 46)	34 (26, 47)	36 (26, 48)	<0.001
Serum calcium ± s.d., mg/dl	8.9 ± 0.4	8.9 ± 0.4	8.9 ± 0.4	8.9 ± 0.4	0.91
Phosphorus ± s.d., mg/dl	3.6 ± 0.5	3.5 ± 0.5	3.6 ± 0.5	3.5 ± 0.5	0.02

25 (OH) vitamin D, 25-hydroxyvitamin D; ACE, angiotensin-converting enzyme; aPWV, arterial pulse wave velocity; ARB, angiotensin receptor blocker; BMI, body mass index; bpm, beats/min; chol., cholesterol; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PTH, parathyroid hormone; SBP, systolic blood pressure.

[a]Median (interquartile range).

Table 2

Association of serum markers of mineral metabolism with pulse wave velocity in older persons

	25-OH-Vitamin D[a]	Intact PTH[a]	Phosphorus[a]	Calcium[a]
	***β* (95% CI) *P* value**	***β* (95% CI) *P* value**	***β* (95% CI) *P* value**	***β* (95% CI) *P* value**
Model 1 unadjusted	−2.86 (−4.38, −1.31) <0.001	3.04 (1.42, 4.68) <0.001	−2.37 (−3.90, −0.81) <0.001	0.52 (−1.01, 2.08) 0.51
Model 2[b]	−2.05 (−3.65, −0.42) 0.01	2.70 (1.09, 4.34) 0.001	−1.86 (−3.46, −0.25) 0.02	0.45 (−1.11, 2.04) 0.57
Model 3[c]	−0.93 (−2.57, 0.73) 0.27	1.43 (−0.22, 3.11) 0.09	−2.02 (−3.63, −0.38) 0.02	−0.16 (−1.75, 1.46) 0.85
Model 4[d]	−0.86 (−2.46, 0.77) 0.30	1.00 (−0.61, 2.64) 0.23	−1.77 (−3.35, −0.17) 0.03	−0.76 (−2.31, 0.82) 0.35

There are 3 participants missing vitamin D for a total of 2,266, 1 participant missing PTH for a total of 2,268, and 7 participants missing calcium for a total of 2,262.

25 (OH) vitamin D, 25-hydroxyvitamin D; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PTH, parathyroid hormone; SBP, systolic blood pressure.

[a] Per s.d. greater (25-OH-vitamin D, per 11.8 μg/l greater; intact PTH per 27.7 pg/ml greater, phosphorus per 0.48 mg/dl greater, and calcium per 0.43 mg/dl).

[b] Age, sex, race/ethnicity, field center, and season at Y2 exam.

[c] Model 2 plus eGFR, BMI, smoking, physical activity, diabetes, LDL, HDL, triglycerides, and lipid medication use.

[d] Model 3 plus SBP, DBP, and antihypertensive medication use.

Table 3

Association of mineral metabolism categories with pulse wave velocity

		Unadjusted model	Adjusted model
		β **(95 % CI)** ***P*** **value**	***β*** **(95% CI)** ***P*** **value**
25-Hydroxyvitamin D (μg/l)			
	n (%)		
>30	712 (31)	Reference	Reference
15–30	1,178 (52)	4.34 (0.69, 8.13) 0.02	0.37 (−3.12, 3.99) 0.85
<15	376 (17)	8.53 (3.46, 13.85) <0.001	3.12 (−1.91, 8.41) 0.23
Parathyroid hormone (pg/ml)			
<65	2,059 (91)	Reference	Reference
≥65	209 (9)	8.03 (2.32, 14.07) <0.001	2.48 (−2.95, 8.22) 0.38
Phosphorus (mg/dl)			
<3.00	255 (11)	Reference	Reference
3.00–3.49	679 (30)	−0.001 (−5.39, 5.70) 0.1	3.43 (−2.00, 9.15) 0.22
3.50–3.99	882 (39)	−5.87 (−10.79, −0,69) 0.02	−1.68 (−6.78, 3.7) 0.53
≥4.00	453 (20)	−4.99 (−10.41, 0.79) 0.08	−2.17 (−7.82, 3.82) 0.47
Calcium (mg/dl)			
<8.5	431 (19)	Reference	Reference
8.5–9.0	1,016 (45)	−3.7 (−7.79, 0.57) 0.08	−4.84 (−8.72, −0.81) 0.02
9.1–9.5	669 (30)	0.78 (−3.8, 5.59) 0.74	−1.70 (−6.05, 2.86) 0.46
≥9.5	146 (7)	−1.80 (−8.42, 5.3) 0.61	−6.91 (−13.27, −0.09) 0.05

There are 3 participants missing vitamin D for a total of 2,266, 1 participant missing PTH for a total of 2,268 and 7 participants missing calcium for a total of 2,262.

BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PTH, parathyroid hormone; SBP, systolic blood pressure.

[a] Adjusted for age, gender, race, site, season at Y2 exam, eGFR, smoking, physical activity, BMI, HDL, LDL, triglycerides, diabetes, lipid medication use, SBP, DBP, and antihypertensive medication use.