Phosphorus levels and future coronary calcification in community–dwelling young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) study

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Introduction

- The major objective of this study was to determine whether an association exists between phosphorus levels and coronary artery calcium (CAC) levels in community-dwelling young adults.
- Several observational studies in dialysis populations have shown that high serum phosphate levels are antecedent associations of mortality and cardiovascular events, independently of calcium and parathyroid hormone levels. It seems natural to hypothesize, therefore, that this relationship also applies within the normal range of phosphorus levels, even in the presence of normal kidney function.
- CAC measures the calcified component of atherosclerotic plaque and is believed to accurately reflect the overall burden of atherosclerosis and to exhibit dose-response relationships with the incidence of future cardiovascular events.

Methods

- CARDIA is an ongoing prospective, multicenter, observational study of cardiovascular disease in young adults. Initially, 5,115 participants, aged 18 to 30 years, were studied between 1985 and 1986 in Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. A random sampling scheme was used to ensure that population-based samples were balanced within centers by age, race, sex, and education level.
- An Imatron (South San Francisco, California) C-150 electron beam scanner, a GE (Fairfield, Connecticut) Lightspeed multidetector scanner, or a Siemens (Berlin, Germany) VZ multidetector scanner was used for computed tomography (CT) scanning of the coronary arteries.
- The analysis was restricted to subjects with CT scans at year 15. Linear regression was used to examine the associations of baseline serum phosphorus levels. Logistic regression was used to examine the association between baseline phosphorus levels and CAC 15 years later.

Results

- Table 1 shows the baseline characteristics of the 3,015 participants who underwent coronary CT scanning. The mean phosphate level was 3.6 mg/dL; calcium, 9.5 mg/dL; and calcium-phosphate product 26.3 mg^2/dL^2. The mean estimated glomerular filtration rate was 116.6, and values for 0.2% of participants were below 60.
- Multivariate associations of serum phosphate (Table 2) included younger age, female sex, African American race, family history of myocardial infarction, low body mass index, HDL-cholesterol, triglycerides, and lower systolic blood pressure.
- At year 15, 3.2% of the study population had minimal CAC, 4.8% had mild CAC, 1.1% had moderate CAC, and 0.5% had severe CAC (Figure 1). Higher phosphate levels were associated with a greater likelihood of higher CAC categories (adjusted odds ratio 1.18 per 0.5 mg/dL, P = 0.0208. Multivariate P-spline plot analysis (Figure 2) suggested that phosphorus levels above 3.9 mg/dL were associated with greater likelihood of CAC ≥ 100.

Table 1. Baseline characteristics at study inception (N=3015)

P (mg/dL)	3.6
Ca (mg/dL)	9.5
Ca-P product (mg^2/dL^2)	26.3
Age (years)	25.2
Female sex (%)	54.4
Race (%)	
White	55.0
African American	45.0
Education < 12 years (%)	7.2
Cigarette smoker (%)	26.5
Hypertension (%)	8.9
Diabetes (%)	0.8
Family history of MI (%)	14.1
Body mass index (kg/m^2)	24.3
LDL-cholesterol (mg/dL)	109.9
HDL-cholesterol (mg/dL)	53.3
Triglycerides (mg/dL)	72.3
Glucose (mg/dL)	82.3
Systolic BP (mm Hg)	110.2
Diastolic BP(mm Hg)	68.5
eGFR	116.6

Table 2. Baseline serum phosphate: multivariate associations.

	Beta	P	
Age (per 3.6 years)	-0.08	< 0.0001	
Female sex (%)	0.07	0.0002	
African American race	0.11	< 0.000	
Family history of MI	0.08	0.0014	
BMI (per 4.4 kg/m^2)	24.3	-0.04	< 0.0001
HDL (per 13.0 mg/dL)	0.04	< 0.0001	
Triglycerides (per 48.7 mg/dL)	0.03	0.0011	
Systolic BP (mm Hg)	-0.06	<0.0001	

Figure 1. Cumulative frequency distribution (%) of coronary artery calcium (CAC) scores at year 15. The dotted vertical lines define the following categories: minimal calcification, 3.2%; mild calcification, 4.8%; moderate calcification, 1.1%, and severe calcification, 0.5%.

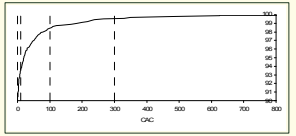
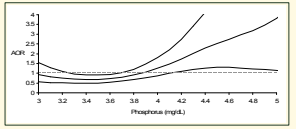


Figure 2. Spline plot relating adjusted odds ratio (AOR, with 95% confidence intervals) of CAC ≥ 100 and serum phosphorus levels. Adjusted for all variables in Table 1 except calcium-phosphorus product and diastolic blood pressure.



Conclusions

- Phosphate levels in the normal range may be risk factors for coronary artery atherosclerosis in community-dwelling young adults. Intervention trials may be indicated to ascertain the causality of this association.

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