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PHASE ANGLE PREDICTS ARTERIAL STIFFNESS AND VASCULAR CALCIFICATION IN PERITONEAL DIALYSIS PATIENTS

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♦ ***Objectives:*** **Fluid overload (FO) is frequently present in peritoneal dialysis (PD) patients and is associated with markers of malnutrition, inflammation, and atherosclerosis/calcification (MIAC) syndrome. We examined the relationships in stable PD patients between phase angle (PhA) and the spectrum of uremic vasculopathy including vascular calcification and arterial stiffness and between PhA and changes in serum fetuin-A levels.**

♦ ***Methods:*** **Sixty-one stable adult PD patients were evaluated in a cross-sectional study (ST1). Phase angle was measured by multifrequency bioimpedance analysis (InbodyS10, Biospace, Korea) at 50 kHz. Augmentation index (AI), a surrogate marker of arterial stiffness, was assessed by digital pulse amplitude tonometry (Endo PAT, Itamar Medical, Caesarea, Israel). Vascular calcification was assessed by simplified calcification score (SCS). Serum fetuin-A levels were measured by ELISA (Thermo scientific; Waltham, MA, USA). Serum albumin was used as a nutritional marker, and serum C-reactive protein (CRP) was used as an inflammatory marker. The same assessments were carried out longitudinally (ST2) in the first 33 patients who completed 1 year of evaluation in ST1.**

♦ ***Results:*** **In ST1, patients with PhA < 6° had higher CRP levels, AI, and SCS and lower serum albumin and fetuin-A levels, in comparison with patients with PhA ≥ 6°. In addition, PhA was a predictor of both AI (β = -0.351, p = 0.023) and SCS ≥ 3 (EXP (B) = 0.243, p = 0.005). In ST2, the increase of PhA over time was associated with decreases in both AI (r = -0.378, p = 0.042) and CRP levels (r = -0.426, p = 0.021), as well as with the increase in serum fetuin-A levels (r = 0.411, p = 0.030).**

♦ ***Conclusions:*** **Phase angle predicts both arterial stiffness and vascular calcification in stable PD patients.**

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Cardiovascular (CV) disease events associated with uremic cardiomyopathy and vasculopathy are the leading cause of morbidity and mortality in patients with chronic kidney disease (CKD), including those on peritoneal dialysis (PD) (1). In addition to an increased prevalence of traditional CV risk factors, there is a wide array of nontraditional factors with negative effects on CV health among the CKD population (2). Fluid overload (FO) is a common condition linked to increased morbidity and mortality in PD patients (3), and effective salt and water management improves survival in this population (4). Fluid overload has been related to uremic cardiomyopathy, namely by the association with hypertension, left ventricular hypertrophy, and heart failure (5–7). Nevertheless, there might be effects beyond traditional risk factors that link FO to CV death among PD patients. It has been suggested that FO contributes to increased arterial stiffness in patients with CKD stages 3 to 5 (8,9) as well as in hemodialysis patients (10). In addition, the association between FO and markers of malnutrition, inflammation, and atherosclerosis/calcification (MIAC) syndrome (11–13), which is in itself a risk factor for mortality in the CKD population, was reported in patients undergoing PD. On the other hand, the association between MIAC syndrome and a deficiency of serum fetuin-A, a well-recognized inhibitory factor of calcification (14–16), was recently reported in PD patients (17).

In the present study, we examined the relationships in stable PD patients between PhA, a composite marker influenced by hydration status and body cell mass integrity, and the spectrum of uremic vasculopathy including vascular calcification and arterial stiffness and between PhA and changes in serum fetuin-A levels.

MATERIALS AND METHODS

SAMPLE

Patients aged 18 years or older who had been undergoing chronic PD for the treatment of end-stage CKD for at least 45 days were invited to participate in the study. Patients with

a recent history (less than 3 months) of infection or an acute CV episode were excluded. The study protocol was approved by the Ethics Committee for Health and Institutional Review Board of our Hospital Centre.

Sixty-one PD patients were included in a cross-sectional study (ST1). Patients were instructed to bring 24-hour dialysate and urine collection, and fasting plasma samples were obtained. In addition, body composition including PhA, arterial stiffness, and vascular calcification were assessed. Similar clinical assessments were carried out longitudinally in a subset of patients included in ST1, 1 year after the first evaluation (ST2). Patients enrolled in the ST2 study were the first 33 to complete 1 year after assessment in ST1.

ASSAYS

Routine laboratory testing of blood, dialysate, and 24-hour urinary samples were performed by a local laboratory using standard procedures. We used renal creatinine clearance (mL/min/1.73 m^2) as a measure of residual renal function (RRF). The presence of RRF was defined as renal creatinine clearance > 0. The Charlson Comorbidity Index (CCI) based on comorbid conditions with varying assigned weights and resulting in a composite score (18) was calculated for all patients. Serum fetuin-A levels were determined using a human fetuin-A enzyme-linked immunosorbent assay (ELISA) kit (Thermo Scientific; Waltham, MA, USA), in duplicate.

ARTERIAL STIFFNESS

Arterial stiffness was evaluated by peripheral arterial tonometry based on a plethysmographic device (EndoPAT2000, Itamar-Medical, Caesarea, Israel) (19). Augmentation index (AI) is a validated surrogate measure of central arterial stiffness that estimates the relative increase that peripherally reflected arterial pressure waves contribute to the forward arterial pressure wave during systole and has been shown to be an independent marker of morbidity and mortality in patients with CKD (20). The augmentation index was calculated from the waveform using the following formula: (P2 – P1)/P1, where P2 is the late systolic peak pressure, representing the composite of the forward arterial pressure wave and the reflected arterial pressure wave and P1 is the early systolic pressure wave, representing the forward arterial pressure wave alone (19). Since heart rate has been shown to strongly influence AI (21), values were corrected to a heart rate of 75 beats per minute.

VASCULAR CALCIFICATION

A simple vascular calcification score (SCS) was calculated in all patients at baseline by a single observer blind to clinical data, in plain X-ray films of pelvis and hands performed in the same center using a validated method previously described by Adragão *et al.* (22). The pelvis films were divided into 4 sections by a horizontal line over the upper limit of both femoral heads and a median vertical line over the vertebral column. Hands films were divided by horizontal lines over the upper limit of the metacarpal bones. Pelvis films evaluated iliac and femoral arteries (ileo-femoral score) whereas hands films evaluated radial and digital arteries (hands score). Any vascular calcification lining the vessel walls, either in an irregular pattern or in a linear pattern, was considered. The presence of vascular calcification in each section was rated as 1 and its absence as 0. The total SCS was the sum of all sections and ranged from 0 to 8. Vascular calcification was classified as prominent when SCS ≥ 3 (22).

BODY COMPOSITION

Body composition including PhA was assessed by multifrequency bioimpedance analysis (BIA) using InBody S10 (Biospace, Seoul, Korea). Multifrequency bioimpedance analysis was validated against available gold standard reference methods to monitor the hydration status in healthy subjects as well as in both hemodialysis and PD patients (23,24).

Bioimpedance measurements were obtained at a frequency of 50 Hz, with the patient in supine position and after drainage of PD fluid. The software analysis assessed the following parameters: impedance (R), reactance (Xc), total body water (TBW), intracellular water (ICW), extracellular water (ECW), ECW/TBW ratio (nECW), segmental fluid distribution, and fat-free mass (FFM). Phase angle is visualized as the slope of the R/Xc vector and decreases with a loss in cell mass as well as with an increase in ECW content (25–27). Since PhA is a composite marker influenced by both hydration status and body cell mass/integrity, a PhA < 6° may reflect both FO and a malnutrition/wasting status. Our study population was divided according to the PhA in 2 groups, PhA ≥ 6° and PhA < 6°. The cutoff value was selected based on previous data from the literature (10,27,28).

STATISTICAL ANALYSIS

Results were expressed as frequencies and percentages for categorical variables. All variables were tested for normal distribution using the Kolmogorov–Smirnov test. For continuous variables, we present mean and standard deviation (SD) for those with normal distribution and median and interquartile range (IR) otherwise. C-reactive protein required log-transformation (*ln*CRP) in order to present a normal distribution.

The baseline characteristics of the 2 study groups with PhA < 6° and ≥ 6° were compared using χ^2 test for categorical variables and Student's *t*-test or Mann-Whitney U-test for continuous variables. The associations between pairs of continuous variables were measured using Pearson's or Spearman's correlation coefficients. Multivariate analysis using multiple linear regression models was performed to analyze the determinants of serum albumin, *ln*CRP and PhA.

Three hierarchical logistic regression models were used to determine predictors for both AI and SCS ≥ 3. Hierarchical regression is a statistical method that explores

the relationships between a dependent variable and several independent variables. In hierarchical regression, the independent variables enter the analysis on a block sequence. The contribution of each variable is ranked, and the variables with lower contribution to the model are sequentially eliminated whereas those remaining in the final model are those that best predict the dependent variable. In ST2, we compared laboratory and clinical characteristics of the studied population using *t*-test or Wilcoxon, as appropriate. To estimate the contribution of changes in PhA to changes in AI, a stepwise forward logistic regression was undertaken. Statistical analysis was performed using SPSS, version 21.0, for Windows (IBM SPSS, Chicago, IL, USA). The null hypothesis was rejected when $p < 0.05$.

RESULTS

CROSS-SECTIONAL STUDY (ST1)

The study sample consisted of 61 patients with a mean age of 48 ± 13 years; 56% were men; 100% were white; 93.4% were on continuous ambulatory PD (CAPD) and 6.1% on automated PD (APD). The median dialysis vintage was 3.5 months (1.7 – 8.3 months). Residual renal function was present in 95% of participants. Overall, 55.7% (n = 34) of the study sample presented PhA < 6°, and the other 44.3% (n = 27) presented PhA ≥ 6° (10,27,28). As expected, a strong correlation was observed in the study population between PhA and nECW (r = -0,873; $p < 0.001$).

Demographic, clinical, and laboratory characteristics of the 2 groups are presented in Table 1. The 2 groups were similar with regard to age, sex, blood pressure, RRF, serum Ca, serum Pi (phosphate) and intact parathyroid hormone (iPTH). In addition, no significant differences were observed between the 2 groups in terms of ECW, ICW, TBW, and FFM. Patients with PhA < 6° had higher CRP levels, nECW, AI, and SCS, as well as lower serum albumin and fetuin-A levels. The prevalence of diabetes was 35.3% in patients with PhA < 6° and 3.7% in patients with PhA ≥ 6°. In addition, SCS proved to be a predictor of PhA independently of fetuin-A levels, *ln*CRP, serum albumin, and AI (β = -0.425; $p = 0.001$).

In order to analyze the relationship between PhA and both serum albumin and *ln*CRP, we performed a multivariate analysis. Using multiple linear regression models, PhA proved to be a predictor of both serum albumin and *ln*CRP, independently of age, serum urea, UF volume, RRF, FFM, and CCI score (Table 2). Using nECW in the analysis instead of PhA yielded similar results (data not shown).

To determine predictors of AI, 3 hierarchical logistic regression models were used (Table 3). In model 1, including age, sex, diabetes, and dialysis vintage, age was the only predictor of AI. In model 2, including age, systolic and diastolic blood pressure, ultrafiltration (UF) volume, RRF, and PhA, both age and PhA were predictors of AI. In model 3, including age, PhA, UF volume, serum calcium, serum phosphate, iPTH, *ln*CRP, serum albumin, and serum fetuin-A, although age was the only AI predictor, UF volume, fetuin-A, and PhA remained in the model. Using nECW in the analysis instead of PhA yielded similar results (data not shown).

To determine predictors of SCS ≥ 3, 3 hierarchical logistic regression models were also used (Table 4). In model 1, including age, sex, diabetes, and dialysis vintage, diabetes was the only predictor of SCS ≥ 3. In model 2, including diabetes, systolic and diastolic blood pressure, UF volume, RRF, and PhA, only PhA was a predictor of SCS ≥ 3. In model 3, including diabetes, PhA, serum calcium, serum phosphate, iPTH, *ln*CRP, serum albumin, and serum fetuin-A, although PhA was the only predictor of SCS ≥ 3, both fetuin-A and diabetes remained in the model. Using nECW in the analysis instead of PhA yielded similar results (data not shown).

LONGITUDINAL STUDY (ST2)

The first 33 patients who completed a year after the evaluation in ST1 (54.2% male; mean age of 47.8, SD = 12; 100% on CAPD) were reassessed to examine longitudinal changes in PhA and their association with markers of uremic vasculopathy and inflammation. Clinical and laboratory characteristics of the ST2 study sample are shown in Table 5. A significant decrease was observed over time in RRF (Table 5). This was accompanied by significant increases in serum albumin, arm muscle circumference, and PhA. However, no significant changes were observed between the 2 evaluation periods in fetuin-A levels, *ln*CRP, AI, SCS, ECW, ICW, or TBW (Table 5).

Phase angle negatively correlated with AI (r = -0.400, p = 0.026; r = -0.643, p = 0.045, respectively) as well as with SCS (r = -0.400, p = 0.026; r = -0.624, p = 0.004, respectively) on both evaluation periods. In unadjusted analysis, the changes in PhA over time were positively correlated with changes in fetuin-A levels (r = 0.411, p = 0.030) and negatively correlated with changes in both AI (r = -0.378, p = 0.042) and *ln*CRP levels (r = -0.426, p = 0.021) (Figure 1). In addition, changes in fetuin-A levels over time were negatively associated with changes in AI (r = -0.395, p = 0.042).

To estimate the contribution of changes in PhA to changes in AI, a stepwise forward logistic regression model was created that included changes in serum calcium, serum phosphate, iPTH, RRF, UF volume, and blood pressure (data not shown). Of all the variables included, only changes in PhA were significantly associated with changes in AI (β = -0.415, p = 0.044). This significance was lost when fetuin-A, *ln*CRP, and serum albumin were included in the model (β = -0.264, p = 0.196).

DISCUSSION

The results of the present study confirm that PhA, a composite marker influenced by both hydration status and body cell mass/integrity, is independently associated with markers of malnutrition and inflammation in patients undergoing PD (29,30). The main new finding of the present study

TABLE 1
Demographic, Clinical, and Laboratory Characteristics in 2 Groups of Stable PD Patients Presenting PhA<6° and PhA≥6° in the Cross-Sectional Study

	PhA<6° (*n*=34)	PhA≥6° (*n*=27)	*p* value
Age (years)[a]	50±14	44±10	0.056
Sex (male)	62%	48%	0.288
Clinical data			
Peritoneal dialysis vintage (months)[b]	3.3 (1.5–5.3)	3.6 (2.8–18.0)	0.139
Diabetes (%)	44%	3.7%	<0.001
Diabetes vintage (years)[a]	17.8±10.4	1	0.143
Hypertension (%)	88%	81%	0.460
Hypertension vintage (years)[a]	12.2±9.4	11.3±8.1	0.713
CAPD/APD	32/2	25/2	
Ultrafiltration volume (mL)[b]	550 (0–925)	400 (0–700)	0.329
RRF (mL/min/1.73 m^2)[a]	3.5±2.2	4.3±2.3	0.155
CCI score[b]	4 (2–6)	2 (2–4)	<0.001
Laboratory values			
Albumin (g/dL)[a]	3.5±4.1	3.8±3.5	0.003
Calcium (mEq/L)[a]	4.4±0.3	4.5±0.4	0.418
Phosphate (mg/dL)[a]	4.7±1.1	4.5±1.2	0.512
iPTH (pg/mL)[a]	441.4±257.2	404.9±256.5	0.584
CRP (mg/L)[b]	3.6 (1.6–10.4)	1.9 (1.3–5.1)	0.041
Fetuin-A (g/L)[a]	0.557±0.251	0.940±0.467	<0.001
Endothelial function (Endo-PAT)	(*n*=26)	(*n*=16)	
AI[a]	18.6±20.6	5.4±18.5	0.031
Vascular calcification score[b]	3 (1–4)	1 (0–2)	<0.001
Vascular calcification score ≥3 (%)	56%	11%	<0.001
Body composition			
ECW (L)[a]	14.7±2.8	15.3±3.2	0.457
ICW (L)[a]	23.3±4.6	25.6±5.3	0.074
TBW (L)[a]	38.0±7.5	40.9±8.5	0.161
ECW/TBW (nECW) (L)[a]	0.386±0.010	0.374±0.011	<0.001
FFM (kg)[a]	51.8±10.1	56.1±11.7	0.138
AMC (cm)[a]	24.3±2.3	26.9±3.7	0. 045

PD = peritoneal dialysis; PhA = phase angle; CAPD = continuous ambulatory PD; APD = automated PD; RRF = residual renal function; CCI = Charlson comorbidity index; iPTH = intact parathyroid hormone; CRP = C-reactive protein; AI = augmentation index; ECW = extracellular water; ICW = intracellular water; TBW = total body water; FFM = fat-free mass; AMC = arm muscle circumference.
Values are expressed as frequencies and percentages for categorical variables.
[a] Values are expressed as mean±SD.
[b] Values are medians with interquartile range in parentheses.

was that PhA also predicted both vascular calcification and arterial stiffness in stable PD patients, suggesting that the decrease of PhA may be linked to uremic vasculopathy in this population.

Fluid overload has been recognized as an important modifiable risk factor that contributes to CV events and all-cause mortality in CKD patients including those undergoing PD (6,8). Actually, the EuroBCM study, carried out in 6 European countries on 639 PD patients, reported that FO was present in 53.4% of the study sample (31). In agreement with the observation by Van Biesen *et al.* (2011), we found that about half of our studied PD patients presented PhA < 6°, which was associated with a significant increase in nECW. Because clinical findings do not allow a reliable quantification of a deviation of euvolemia in PD patients, our results reinforce the importance of a routine assessment of hydration status by BIA in this population (32).

It should be mentioned, however, that PhA is a composite marker influenced by both hydration status and body cell mass/integrity. The finding that arm muscle circumference was reduced in the group with PhA < 6° suggests that malnutrition/wasting also is likely involved in the reduction of PhA in our PD population.

The association between FO and malnutrition-inflammation has previously been reported in PD patients (11,29,30). Accordingly, a close relationship was observed in the present study between PhA and markers of malnutrition and inflammation. In the multivariate analysis, this relationship was shown

TABLE 2
Predictive Variables of C-Reactive Protein and Serum Albumin in the Cross-Sectional Study According to Multiple Linear Regression Analysis (*n*=61)

Variable	C- reactive protein β	*p*	Serum albumin B	*p*
Age (years)	0.186	0.282	-0.184	0.335
Ultrafiltration volume (mL)	0.005	0.972	0.156	0.318
Serum urea (mg/dL)	-0.242	0.115	0.152	0.366
RRF (mL/min/1.73 m^2)	-0.041	0.748	0.045	0.752
FFM (kg)	0.245	0.096	0.057	0.723
CCI score	-0.016	0.923	0.086	0.645
PhA (°)	-0.419	0.003*	0.302	0.047*

RRF = residual renal function; FFM = fat-free mass; CCI = Charlson comorbidity index; PhA = phase angle; β = standardized regression coefficient.
* $p<0.05$

TABLE 3
Predictive Variables of Arterial Stiffness (AI, *n*=47) in the Cross-Sectional Study According to Linear Hierarchical Regression Analysis

	β	*p*
Model 1 (R^2=0.158)		
Age (years)	0.364	0.017
Model 2 (R^2=0.267)		
Age (years)	0.361	0.023
Ultrafiltration volume (mL)	-0.273	0.083
PhA (°)	-0.351	0.023
Model 3 (R^2=0.323)		
Age (years)	0.384	0.014
Ultrafiltration volume (mL)	-0.262	0.088
PhA (°)	-0.266	0.088
Fetuin-A levels (g/L)	-0.249	0.085

PhA = phase angle; R^2 = coefficient of determination; β = standardized regression coefficient; iPTH = intact parathyroid hormone.
Model 1. Variables included: age, sex, diabetes, dialysis vintage.
Model 2. Variables included: age, systolic and diastolic blood pressure, ultrafiltration volume, residual renal function, PhA.
Model 3. Variables included: age, ultrafiltration volume, PhA, serum calcium, serum phosphate, iPTH, C-reactive protein, serum albumin, serum fetuin-A.

to be independent of age, serum urea, UF volume, RRF, FFM, and CCI score. In addition, in the longitudinal study, we found that changes in PhA were negatively associated with changes in CRP and positively associated with changes in fetuin-A levels over time, thus reinforcing the existence of a dynamic relationship between PhA and inflammation. The relationship between FO and inflammation was suggested to be bidirectional (30). Fluid overload may be one of the factors implicated in inflammation in patients undergoing PD, but also, an inflammatory process

TABLE 4
Predictive Variables of Simplified Calcification Score ≥3 (SCS, *n*=61) in the Cross-Sectional Study According to Linear Hierarchical Regression Analysis

	EXP (B)	*p*
Model 1 (R^2=0.484)		
Diabetes	8.800	0.002
Model 2 (R^2=0.563)		
Diabetes	2.394	0.282
PhA (°)	0.255	0.003
Model 3 (R^2=0.527)		
Diabetes	2.273	0.331
PhA (°)	0.243	0.005
Fetuin-A levels (g/L)	0.268	0.119

PhA = phase angle; SCS = simple calcification score; R^2 = Nagelkerke coefficient of determination; iPTH = intact parathyroid hormone.
Model 1. Variables included: age, sex, diabetes, dialysis vintage.
Model 2. Variables included: diabetes, systolic and diastolic blood pressure, ultrafiltration volume, residual renal function, PhA.
Model 3. Variables included: diabetes, PhA, serum calcium, serum phosphate, iPTH, C-reactive protein, serum albumin, serum fetuin-A.

itself can contribute to FO indirectly (30). Inflammation is associated with increased peritoneal permeability, which in turn can lead to fluid retention due to loss of osmotic gradient (33). The observation that diabetes was present in 35.3% of patients with PhA < 6° but in only 3.7% of those with PhA ≥ 6° fits well with the importance of diabetes as a cause of both FO and inflammation in PD patients (34).

In the present study, we found that PhA predicted both vascular calcification and arterial stiffness in stable PD patients. In addition, the increase of PhA over time was closely associated with the decrease in arterial stiffness, thus suggesting the existence of a dynamic relationship between PhA and arterial stiffness in PD patients. Our data are in agreement with the observation in hemodialysis patients that short-term fluid removal during a single dialysis session is accompanied by partial correction of increased arterial stiffness to levels indistinguishable from those recorded in euvolemic patients (10).

Although the pathophysiology of uremic vasculopathy is far from being fully understood, a central role for mineral and bone abnormalities/vascular calcifications is currently accepted (35). Emerging evidence points to the role of inflammation in reducing the natural defenses that prevent extra-skeletal calcification, in part through reduction in serum fetuin-A, a circulating inhibitor of extra-skeletal calcification (14–17). In ST1, we found that fetuin-A levels were significantly lower in patients with a PhA < 6°, and, interestingly, in ST2, the increase of PhA was associated with the increase in fetuin-A levels.

The main limitations of the present study are that this was an observational study with a relatively small sample size and we cannot establish the causality of the relationships observed between PhA and the spectrum of uremic vasculopathy. In addition, we did not request that participants stop taking

TABLE 5
Clinical and Laboratory Parameters During the 1st and 2nd Evaluation Periods in the Longitudinal Study Sample (*n*=33)

Variable	1st evaluation	2nd evaluation	*p*
24-hour urine volume (mL)[b]	1,850 (975–2,325)	1,050 (387–1,578)	<0.001
24-hour dialysate volume (mL)[b]	6,340 (5,727–7,092)	9,217 (6,692–12,585)	<0.001
Ultrafiltration volume (mL)[b]	300 (-175–800)	600 (100–1,300)	0.205
RRF (mL/min/1.73 m^2)[a]	4.17±1.9	2.26±1.8	<0.001
Laboratory Values			
Albumin (g/dL)[a]	35.7±3.8	36.9±3.8	0.023
Calcium (mEq/L)[a]	4.4±0.3	4.3±0.5	0.382
Phosphate (mg/dL)[a]	4.7±1.0	4.7±1.0	0.839
iPTH (pg/mL)[a]	433.5±244.7	472±270.9	0.586
CRP (mg/L)[b,c]	1.9 (1.4–4.8)	2.4 (1.1–5.7)	0.439
Fetuin-A (g/L)[a]	0.645±0.464	0.830±0.573	0.078
Endothelial function (Endo-PAT)			
AI[a]	11.7±23.6	10.8±24.6	0.814
Vascular calcification score[a]	1.3 (0–8)	1.3 (0–8)	0.999
Body composition			
ECW (l)[a]	14.7±2.9	15.7±4.2	0.238
ICW (l)[a]	23.9±5.2	24.3±5.8	0.490
TBW (l)[a]	38.6±8.1	40.0±8.1	0.159
ECW/TBW (nECW)[a]	0.383±0.130	0.380±0.130	0.025
FFM (kg)[a]	52.9±11.1	54.3±11.3	0.237
PhA (°)[a]	5.6±1.4	6.0±1.1	0.021
AMC (cm)[a]	24.5±2.4	27.2±3.3	<0.001

RRF = residual renal function; iPTH = intact parathyroid hormone; CRP = C-reactive protein; AI = augmentation index; ECW = extracellular water; ICW = intracellular water; TBW = total body water; FFM = fat-free mass = PhA = phase angle; AMC = arm muscle circumference.
[a] Values are expressed as mean±SD.
[b] Values are medians with interquartile range in parentheses.
[c] *p* value was obtained using the transformed variable.

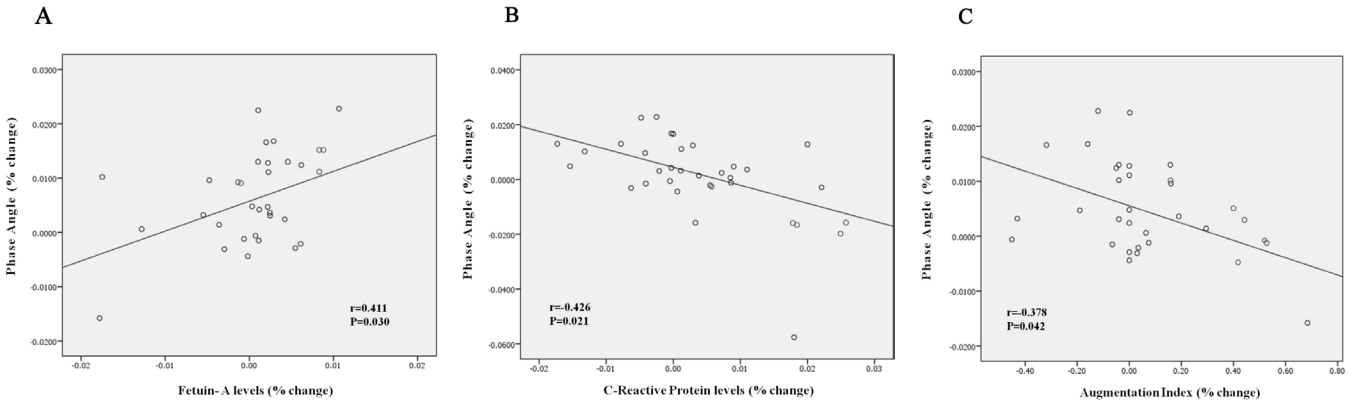

Figure 1 — Scatter plots depict the associations of changes in PhA with changes in fetuin-A levels (A), C-reactive protein levels (B), and AI (C) in the longitudinal study (*n*=33). PhA = phase angle; AI = augmentation index.

vasoactive blood pressure medications on the day of AI measurement, and thus we cannot exclude that this may have influenced the results.

The strengths of our study include the adjustment, by multivariate and hierarchical regression analysis, for variables that may influence vascular calcification and arterial stiffness in stable PD patients. Moreover, we were able to study longitudinal changes in PhA in a subset of PD patients and their association with the spectrum of uremic vasculopathy and inflammation including fetuin-A levels.

We conclude that PhA, a composite marker influenced by hydration status and body cell mass/integrity, predicts both arterial stiffness and vascular calcification in stable PD patients. Further studies will determine whether effective

strategies guided by control of FO in PD patients contribute to improvement of uremic vasculopathy.

DISCLOSURES

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