

Longitudinal Associations Between Phase Angle and Changes in Weight and Body Composition: Evidence from the Iranian National Obesity Registry

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Abstract

Phase angle (PhA) is an indicator of cellular membrane integrity. We aimed to investigate the longitudinal association between PhA change and changes in weight and body composition, stratified by demographic and clinical factors, using data from the Iranian National Obesity Registry. This retrospective cohort study included 6046 individuals. Body composition data were collected using an InBody 770 bioimpedance analyzer. Repeated measures correlation and mixed-effects models were used in R (version 4.3.3). PhA significantly correlated with weight ($r = 0.26$, $p < 0.001$), fat mass ($r = 0.26$, $p < 0.001$), skeletal muscle mass ($r = 0.25$, $p < 0.001$), and intracellular water content ($r = 0.25$, $p < 0.001$). A strong negative correlation was observed with the extracellular water/total body water ratio (ECW/TBW) ($r = -0.76$, $p < 0.001$). Linear mixed models confirmed these correlations, with ECW/TBW showing the strongest association (estimate = -0.63 ; 95% CI: -0.65 , -0.62). PhA was associated with weight (estimate = 0.013 ; 95% CI: 0.012 , 0.014), varying by sex, age, BMI, intervention type, and time. Notably, stronger associations were observed in women (estimate = 0.014 ; 95% CI: 0.014 , 0.015), older adults (estimate = 0.018 ; 95% CI: 0.015 , 0.019), and underweight individuals (estimate = 0.02 ; 95% CI: 0.020 , 0.025). The rate of PhA change with weight change may be higher in females and older adults but lower in individuals with obesity and over longer intervals.

Introduction

Bioimpedance analysis (BIA) has become widely accepted as a practical, non-invasive technique for measuring body composition. By estimating total body water (TBW), BIA measures fat-free mass (FFM), body fat mass (BFM), body cell mass, and phase angle (PhA) ^[1]. Among these parameters, PhA has gained attention as a sensitive indicator of cellular health and membrane integrity ^[2, 3]. Unlike conventional anthropometric measures, it provides deeper insight into muscle quality and overall body composition ^[4, 5]. Higher PhA values reflect better cellular function, greater muscle mass, lower BFM and better physical fitness ^[6, 7]. Consequently, PhA has been increasingly utilized in clinical and research settings to assess nutritional status, particularly in people with obesity or underweight individuals. The physiological basis of PhA lies in its ability to reflect the balance between the intracellular and extracellular water compartments ^[8]. PhA is influenced by cellular membrane integrity and body composition; greater amounts of lean tissue and intracellular water typically correspond to higher PhA values. Conversely, increased extracellular water or reduced cellular mass results in lower PhA values, indicating impaired cellular health ^[9]. Factors such as age, gender, and body mass index (BMI) also affect PhA. For example, men generally have higher PhA values because of their greater lean mass. PhA tends to decrease with age, reflecting the progressive loss of skeletal muscle mass and the accumulation of fat ^[3, 10]. The physiological basis of PhA, particularly its association with cellular hydration and lean body mass, support its value in evaluating both undernutrition and overnutrition. This dual applicability highlights its usefulness for risk identification and for monitoring the effectiveness of interventions across diverse populations. Obesity (BMI ≥ 30) represents a growing global health challenge characterized not only by excess body fat but also by alterations in skeletal muscle structure

and function ^[11]. These changes are associated with increased risks of noncommunicable diseases such as cardiovascular diseases, type 2 diabetes mellitus, and some cancers ^[12]. Studies on the relationship between PhA and BMI have showed conflicting results. For example, a study showed that an increase in BMI leads to a greater phase angle, which is attributed to the greater presence of muscle and fat cells. Interestingly, this positive correlation was limited to BMI values under 30 kg/m². In contrast, individuals with a BMI above 40 kg/m² showed a negative association ^[13]. On the other hand, other studies reported a negative association between PhA and BMI ^[14, 15]. While BMI is widely used to classify obesity, it does not account for body composition or cellular health ^[16]. By reflecting factors such as hydration, muscle mass, and nutritional status, PhA offers a more precise measure of cellular integrity ^[17].

At the other end of the nutritional spectrum, underweight individuals (BMI < 18.5) also face significant health risks, including nutrient deficiencies, impaired immune function, and increased susceptibility to infections ^[18]. Chronic energy deficiency can lead to muscle wasting and a reduction in bone density, which increases the risk of fractures and osteoporosis ^[19]. Additionally, individuals with underweight may experience hormonal imbalances that can negatively impact reproductive health ^[20]. Over time, these issues can lead to impaired physical function, reduced quality of life, and increased risk of mortality ^[21]. In such cases, PhA monitoring offers valuable insights into the cellular impact of weight gain interventions, enabling clinicians to assess improvements in metabolic and inflammatory parameters during recovery.

The dual utility of PhA in assessing cellular health during weight loss in people with obesity and weight gain in underweight individuals highlights its importance in nutritional research. Unlike traditional measures that rely only on BMI, PhA monitoring may help identify risks of malnutrition, assess improvements in metabolic parameters, and evaluate reductions in inflammation during weight management interventions ^[17]. Despite its potential, evidence linking changes in PhA to weight and body composition over time remains limited. This study aimed to address this gap by investigating the longitudinal association between PhA and weight and body composition in a large Iranian cohort. By stratifying the analysis on the basis of demographic and clinical factors such as age, gender, BMI categories, and intervention types, this research provides novel insights into the dynamic response of PhA to weight fluctuations over time.

Methods

This longitudinal study was performed from 2017 to 2023 on individuals registered in the Iranian National Obesity Registry (IRNOR) in Mashhad. All study procedures were conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of Mashhad University of Medical Sciences in October 2023 (IR.MUMS.Medical.REC.1402.249). All Participants provided informed consent, which was recorded in an electronic registry.

The inclusion criteria were being 18 years of age or older, having at least two documented visits to the nutrition clinic, and experiencing weight change between those visits. The exclusion criteria included pregnancy and contraindications to the use of a BIA device, such as the presence of a pacemaker, implanted artificial devices, or apparent edema. Demographic data, history of using body-contouring devices, and history of following any diet were collected by a nutritionist. Body composition analysis was performed using an InBody 770 device (Biospace Co., Ltd., Seoul, South Korea) by a trained operator. Individuals with missing data in the obesity registry were excluded. The subjects were categorized into groups based on several factors, including type of treatment received (diet only or diet plus body-contouring devices), baseline BMI (underweight, normal weight, overweight, or obesity), sex, time interval (3, 6, 9, or 12 months), age (< 60 years or ≥ 60 years), and type of weight change (weight loss or weight gain). Participants were required to follow these guidelines before using the device to standardize measurements:

1) avoid consuming alcoholic beverages within the previous 12 hours; 2) refrain from consuming caffeinated products within the previous 8 hours; 3) avoid exercise or sauna use within the previous 8 hours; and 4) remove all metal and/or magnetic jewelry, therapeutic magnets, communication devices, and cell phones from the body.

Statistical analysis

Excel 2023 and the R programming language (version 4.3.3) were used for data manipulation and preparation prior to statistical analysis. To classify weight change groups, the difference in body weight between each follow-up visit and the first visit was calculated for each individual. A positive difference was classified as weight gain, whereas a negative difference was classified as weight loss. Absolute and relative frequency tables were used to describe qualitative variables, whereas means and standard deviations were reported for quantitative variables. Given the longitudinal nature of the data, with each participant having at least two visits, the correlation between changes in weight and body composition with PhA changes was analyzed using the *rmc* or *r* package in R. Additionally, to assess the relationship between changes in weight and body composition and changes in PhA, linear mixed-effects models were fitted using the *lme4* package in R. In the models, the ID-number variable was included as a random effect because the relationship between weight and PhA changes was assessed across multiple visits for each individual. To determine the fixed effects included as covariates in the model, variables with the strongest repeated-measures correlations with both phase angle and weight were selected for inclusion in Models 1 and 2. Furthermore, collinearity between weight and the candidate variables was assessed, and those with the lowest collinearity were ultimately selected as covariates in Models 1 and 2. At the end, collinearity was further double-checked using the *vif* () function in R. Finally, three models were examined in all analyses: 1) Raw model, which included weight and PhA; 2) Model 1, adjusted for age, sex, and days after baseline; 3) Model 2, adjusted for age, sex, days after baseline, changes in the extra-cellular water/total body water (ECW/TBW), and waist-to-hip ratio (WHR). R^2 was reported to provide an absolute measure of the goodness-of-fit of a model, with two statistics: marginal R^2 (mR^2 ; i.e., variance explained by fixed effects) and conditional R^2 (cR^2 ; i.e., variance

explained by both fixed and random effects) ^[22]. The statistical significance of the difference between the estimates of the two models was assessed by examining whether their 95% confidence intervals overlapped.

Results

This study included 6,046 participants, 28.7% men (n = 1737) and 71.3% women (n = 4309), with a mean age of 35.5 ± 12.9 years. The mean baseline weight and BMI were 76.75 ± 21.84 kg and 28.84 ± 7.91 kg/m², respectively. BMI categories included 11.7% with underweight, 20.3% with normal weight, 22.6% with overweight, and 45.4% with obesity. Table 1 provides additional demographic and anthropometric characteristics.

Table 1
Baseline characteristics of individuals

Variables		Amount
Age (year)		12.9 $\pm$ 35.5
Gender	Men	1737 (28.7%)
	Women	4309 (71.3%)
Weight (kg)		21.84 $\pm$ 76.75
Body mass index (kg/m ²)		7.91 $\pm$ 28.84
Phase angle (°)		0.71 $\pm$ 5.31
Body fat mass (kg)		15.40 $\pm$ 30.21
Fat mass percentage (%)		37.22 $\pm$ 12.01
Fat free mass (kg)		46.54 $\pm$ 10.47
Skeletal muscle mass (kg)		25.53 $\pm$ 6.31
Soft lean mass (kg)		3.89 $\pm$ 9.91
Visceral fat level		13.75 $\pm$ 7.05
Bone mineral content (kg)		2.65 $\pm$ 0.58
Total body water (kg)		34.21 $\pm$ 7.70
Extracellular water (kg)		13.10 $\pm$ 2.87
Intracellular water (kg)		21.11 $\pm$ 4.84
Extracellular water/Total body water		0.38 $\pm$ 0.007
Basal metabolic rate (kcal)		1375 $\pm$ 226

Variables		Amount
Waist to hip ratio		0.92 ± 0.08
Intervention	Diet + Body contouring	164 (2.7%)
	Only diet	5882 (97.3%)
Body mass index categories	Underweight	706 (11.7%)
	Normal	1230 (20.3%)
	Overweight	1365 (22.6%)
	Obese	2745 (45.4%)
Age groups	Younger than 60	5704 (94.3%)
	60 and older	342 (5.7%)
Weight change	Weight gain	2108 (31.6%)
	Weight loss	4553 (68.4%)
Quantitative data are presented as the mean ± standard deviation, while qualitative data are reported as frequency (percentage).		

Table 2 shows significant positive correlations between changes in PhA and changes in weight ($r = 0.26$, $p < 0.001$), BFM ($r = 0.26$, $p < 0.001$), skeletal muscle mass (SMM) ($r = 0.25$, $p < 0.001$), intra-cellular water (ICW) ($r = 0.25$, $p < 0.001$), and BMI ($r = 0.26$, $p < 0.001$). A strong inverse correlation with ECW/TBW ($r = -0.76$, $p < 0.001$) was also observed. Other measures, including changes in FFM ($r = 0.15$, $p < 0.001$) and visceral fat level ($r = 0.23$, $p < 0.001$), were also significantly correlated with changes in PhA.

Table 2

Repeated measures correlation and linear mixed model analysis of the relationship between phase angle changes and changes in weight and body composition components

Body composition	Repeated measures correlation		Linear mixed-effects models					
	r	p value	Estimate	95% CI	AIC	p value	mR ²	cR ²
Weight	0.26	< 0.001	0.01	0.012, 0.013	10287	< 0.001	0.14	0.93
Fat mass	0.26	< 0.001	0.01	0.011, 0.013	11357	< 0.001	0.06	0.94
Fat free mass	0.15	< 0.001	0.04	0.035, 0.038	9414	< 0.001	0.29	0.92
Skeletal muscle mass	0.25	< 0.001	0.07	0.068, 0.071	8223	< 0.001	0.37	0.93
Fat mass (%)	0.25	< 0.001	0.01	0.009, 0.011	12024	< 0.001	0.02	0.93
Body mass index (BMI)	0.26	< 0.001	0.03	0.028, 0.032	10884	< 0.001	0.09	0.93
Intracellular water (ICW)	0.25	< 0.001	0.09	0.088, 0.093	8223	< 0.001	0.37	0.93
Extracellular water (ECW)	-0.05	< 0.001	0.08	0.080, 0.090	11298	< 0.001	0.13	0.91
Total body water (TBW)	0.13	< 0.001	0.05	0.046, 0.050	9581	< 0.001	0.28	0.92
ECW/TBW (%)	-0.76	< 0.001	-0.63	-0.624, -0.638	8418-	< 0.001	0.56	0.96
Visceral fat level	0.23	< 0.001	0.02	0.019, 0.023	11712	< 0.001	0.04	0.93
Waist/hip ratio (%)	0.32	< 0.001	0.02	0.024, 0.026	10216	< 0.001	0.08	0.94
Soft lean mass	0.16	< 0.001	0.04	0.038, 0.40	9310	< 0.001	0.30	0.92
Bone mineral content	-0.02	< 0.001	0.36	0.343, 0.388	11428	< 0.001	0.10	0.91
Basal metabolic rate	0.15	< 0.001	0.0016	0.0016, 0.0017	9414	< 0.001	0.29	0.92
AIC: Akaike Information Criterion (a measure of model fit that balances goodness-of-fit with model complexity; lower AIC values indicate better models)								

Body composition	Repeated measures correlation	Linear mixed-effects models						
		r	p value	Estimate	95% CI	AIC	p value	mR ²
mR ² : Marginal R ² (the proportion of variance explained by the fixed effects (predictors) in a linear mixed-effects model)								
cR ² : Conditional R ² (the proportion of variance explained by both fixed and random effects in a linear mixed-effects model)								
95%CI: 95% confidence interval								

Linear mixed-effects models (Table 2) revealed that changes in ECW/TBW ratio had the strongest negative association with changes in PhA (estimate = - 0.63, mR² = 0.56, cR² = 0.96). Positive associations were observed for changes in ICW (estimate = 0.09, mR² = 0.37, cR² = 0.93) and SMM (estimate = 0.07, mR² = 0.37, cR² = 0.93). Weaker associations were observed for BFM (estimate = 0.01, mR² = 0.06, cR² = 0.94) and body fat percentage (BFP) (estimate = 0.01, mR² = 0.02, cR² = 0.93).

In the whole population (Table 3), changes in weight were significantly associated with changes in PhA across all models (estimate = 0.013, p < 0.001), with Model 2 providing the best fit (mR² = 0.80, cR² = 0.96, AIC = - 14074). Gender-specific analyses (Table 3) showed that weight changes had a significantly greater effect on PhA changes in women (estimate = 0.014; 95% CI: 0.014, 0.015; mR² = 0.73, cR² = 0.95, AIC = - 12207) than men (estimate = 0.010; 95% CI: 0.009, 0.011; mR² = 0.74, cR² = 0.95, AIC = - 2209). Age-based analyses (Table 3) showed that older adults exhibited a stronger association between changes in weight and PhA (estimate = 0.018; 95% CI: 0.015, 0.019; mR² = 0.77, cR² = 0.95, AIC = - 560) than younger participants (estimate = 0.013; 95% CI: 0.012, 0.013; mR² = 0.78, cR² = 0.96, AIC = - 13424). Both the weight gain and weight loss groups (Table 3) demonstrated significant associations between weight and PhA changes, with weight gain showing a statistically significant stronger effect (estimate = 0.016; 95% CI: 0.015, 0.017) than weight loss (estimate = 0.012; 95% CI: 0.012, 0.013).

Table 3

Linear mixed model analysis of the longitudinal relationship between phase angle and weight in the whole population and subgroups of gender, age, and the kind of weight change

Group		Model	Estimate	Confidence Intervals (95%)	AIC	p value	mR ²	cR ²
Whole population		Raw model	0.013	0.0125, 0.0135	10287	< 0.001	0.14	0.93
		Model 1	0.012	0.0117, 0.0127	8548	< 0.001	0.35	0.93
		Model 2	0.013	0.0128, 0.0136	-14074	< 0.001	0.80	0.96
Gender	Men (n = 1739)	Raw model	0.009	0.008, 0.010	3362	< 0.001	0.10	0.93
		Model 1	0.009	0.009, 0.010	3068	< 0.001	0.21	0.93
		Model 2	0.010	0.009, 0.011	-2209-	< 0.001	0.74	0.95
	Women (n = 4309)	Raw model	0.013	0.012, 0.013	5451	< 0.001	0.15	0.91
		Model 1	0.013	0.013, 0.014	5274	< 0.001	0.17	0.91
		Model 2	0.014	0.014, 0.015	-12207	< 0.001	0.73	0.95
Age	< 60 (n = 5707)	Raw model	0.013	0.0124, 0.0135	9132	< 0.001	0.15	0.93
		Model 1	0.011	0.0107, 0.0117	7465	< 0.001	0.35	0.93
		Model 2	0.013	0.0123, 0.0131	-13424	< 0.001	0.78	0.96
	60 ≤ (n = 357)	Raw model	0.012	0.0093, 0.0151	664	< 0.001	0.12	0.92
		Model 1	0.012	0.0088, 0.0147	653	< 0.001	0.15	0.92
		Model 2	0.018	0.0155, 0.0189	-560	< 0.001	0.79	0.95
Weight change	Weight loss (n = 4553)	Raw model	0.013	0.012, 0.013	7327	< 0.001	0.13	0.93
		Model 1	0.011	0.010, 0.012	6142	< 0.001	0.33	0.93

Group	Model	Estimate	Confidence Intervals (95%)	AIC	p value	mR ²	cR ²
Weight gain (n = 2108)	Model 2	0.012	0.012, 0.013	-10237	< 0.001	0.78	0.96
	Raw model	0.013	0.012, 0.014	4323	< 0.001	0.14	0.93
	Model 1	0.012	0.012, 0.014	3597	< 0.001	0.38	0.93
	Model 2	0.016	0.015, 0.017	-3759	< 0.001	0.85	0.97
Model 1: Adjusted for age, gender, and days after baseline Model 2: Adjusted for age, gender, days after baseline, extracellular water/total body water, and waist/hip ratio AIC: Akaike Information Criterion (a measure of model fit that balances goodness-of-fit with model complexity; lower AIC values indicate better models) mR²: Marginal R² (the proportion of variance explained by the fixed effects (predictors) in a linear mixed-effects model) cR²: Conditional R² (the proportion of variance explained by both fixed and random effects in a linear mixed-effects model)							

Analyses by BMI category (Table 4) indicated that individuals with underweight had the strongest association between changes in weight and PhA (estimate = 0.02; 95% CI: 0.020, 0.025; mR² = 0.85, cR² = 0.98, AIC = - 1898), whereas individuals with obesity exhibited the weakest association (estimate = 0.009; 95% CI: 0.008, 0.009; mR² = 0.75, cR² = 0.96, AIC = - 6952).

Table 4
Linear Mixed Model Analysis of the Relationship between Phase Angle Changes and Weight Changes
across Body Mass Index Categories

BMI	Model	Estimate	Confidence Interval (95%)	AIC	p value	Marginal R ²	Conditional R ²
Underweight (n = 706)	Raw model	0.04	0.039, 0.048	811	< 0.001	0.20	0.94
	Model 1	0.03	0.022, 0.032	588	< 0.001	0.47	0.95
	Model 2	0.02	0.020, 0.025	1898-	< 0.001	0.85	0.98
Normal (n = 1230)	Raw model	0.02	0.020, 0.025	2702	< 0.001	0.07	0.93
	Model 1	0.01	0.013, 0.018	2151	< 0.001	0.43	0.93
	Model 2	0.02	0.018, 0.021	2351-	< 0.001	0.87	0.97
Overweight (n = 1365)	Raw model	0.02	0.015, 0.018	1943	< 0.001	0.05	0.92
	Model 1	0.01	0.009, 0.013	1578	< 0.001	0.31	0.92
	Model 2	0.01	0.014, 0.016	4211-	< 0.001	0.83	0.97
Obese (n = 2745)	Raw model	0.01	0.011, 0.013	4407	< 0.001	0.08	0.92
	Model 1	0.008	0.007, 0.009	3606	< 0.001	0.33	0.92
	Model 2	0.009	0.008, 0.009	6952-	< 0.001	0.75	0.96
Model 1: Adjusted for age, gender, and days after baseline Model 2: Adjusted for age, gender, days after baseline, extracellular water/total body water, and waist/hip ratio AIC: Akaike Information Criterion (a measure of model fit which balances goodness-of-fit with model complexity; lower AIC values indicate better models) Marginal R²: the proportion of variance explained by the fixed effects (predictors) in a linear mixed-effects model Conditional R²: the proportion of variance explained by both fixed and random effects in a linear mixed-effects model							

Intervention-based analysis (Table 5) found that both groups—those following a diet-only approach (estimate = 0.013; 95% CI: 0.012, 0.013; mR² = 0.80, cR² = 0.96, AIC = - 1311) and those combining diet with body contouring (estimate = 0.015; 95% CI: 0.012, 0.017; mR² = 0.76, cR² = 0.96, AIC = - 991)—had significant associations, with no significant difference between them.

Table 5
Linear Mixed Model Analysis of the Relationship between Phase Angle Changes and Weight Changes Stratified by Intervention

Intervention	Model	Estimate	Confidence Intervals (95%)	AIC	p value	Marginal R ²	Conditional R ²
Diet + Body contouring (n = 165)	Raw model	0.014	0.010, 0.017	82	< 0.001	0.08	0.92
	Model 1	0.012	0.008, 0.015	71	< 0.001	0.16	0.92
	Model 2	0.015	0.012, 0.017	991-	< 0.001	0.76	0.96
Only diet (n = 5885)	Raw model	0.013	0.012, 0.013	10204	< 0.001	0.14	0.93
	Model 1	0.012	0.011, 0.012	8470	< 0.001	0.36	0.93
	Model 2	0.013	0.012, 0.013	1311-	< 0.001	0.80	0.96
Model 1: Adjusted for age, gender, and days after baseline							
Model 2: Adjusted for age, gender, days after baseline, extracellular water/total body water, and waist/hip ratio							
AIC: Akaike Information Criterion (a measure of model fit which balances goodness-of-fit with model complexity; lower AIC values indicate better models)							
Marginal R ² : the proportion of variance explained by the fixed effects (predictors) in a linear mixed-effects model							
Conditional R ² : the proportion of variance explained by both fixed and random effects in a linear mixed-effects model							

Finally, analysis of time intervals (Table 6) revealed a consistent direct association between changes in weight and PhA across all intervals, with the strongest estimates observed at 0–6 months (estimate = 0.014; 95% CI: 0.013, 0.015) and 0–9 months (estimate = 0.014; 95% CI: 0.013, 0.015), whereas the 0–12 months interval showed a smaller effect size (estimate = 0.011; 95% CI: 0.009, 0.0128). Figure 1 shows the summary of the longitudinal association of phase angle with weight among all study groups.

Table 6
Linear Mixed Model Analysis of the Relationship between Phase Angle Changes and Weight Changes
Stratified by Time Intervals

Time intervals	Model	Estimate	Confidence Intervals (95%)	AIC	p value	Marginal R ²	Conditional R ²
0–3 months (n = 5465)	Raw model	0.011	0.010, 0.012	9015	< 0.001	0.11	0.94
	Model 1	0.011	0.010, 0.011	7500	< 0.001	0.33	0.94
	Model 2	0.013	0.013, 0.014	7250-	< 0.001	0.89	0.97
0–6 months (n = 927)	Raw model	0.015	0.013, 0.016	312	< 0.001	0.19	0.94
	Model 1	0.013	0.011, 0.014	155	< 0.001	0.32	0.94
	Model 2	0.014	0.013, 0.015	5379-	< 0.001	0.78	0.97
0–9 months (n = 307)	Raw model	0.016	0.014, 0.017	342-	< 0.001	0.20	0.94
	Model 1	0.016	0.014, 0.018	371-	< 0.001	0.31	0.94
	Model 2	0.014	0.013, 0.015	3379-	< 0.001	0.75	0.97
0–12 months (n = 128)	Raw model	0.014	0.012, 0.016	240-	< 0.001	0.15	0.93
	Model 1	0.011	0.009, 0.014	262-	< 0.001	0.24	0.92
	Model 2	0.011	0.009, 0.013	1794-	< 0.001	0.74	0.95
Model 1: Adjusted for age, gender, and days after baseline Model 2: Adjusted for age, gender, days after baseline, extracellular water/total body water, and waist/hip ratio AIC: Akaike Information Criterion (a measure of model fit which balance goodness-of-fit with model complexity; lower AIC values indicate better models) Marginal R²: the proportion of variance explained by the fixed effects (predictors) in a linear mixed-effects model Conditional R²: the proportion of variance explained by both fixed and random effects in a linear mixed-effects model							

Discussion

This study demonstrated a significant positive association between changes in PhA and weight across a large cohort, emphasizing the potential of PhA as a biomarker for monitoring cellular health during weight management interventions. Our findings align with previous studies indicating that PhA is sensitive to alterations in body composition and hydration status, making it a valuable tool for assessing cellular health in individuals with obesity and those with underweight. The strongest inverse association was observed between changes in PhA and ECW/TBW ($r = -0.76$). This finding is consistent with the study by Najafi et al., which reported a similarly strong negative correlation ($r = -0.71$, $p < 0.001$) during weight loss interventions using intermittent fasting [23]. They also examined this association using a model that revealed a negative relationship between changes in ECW/TBW ratio and PhA ($\beta = -0.46$, $R^2 = 0.51$, $p < 0.001$). Studies have shown that with weight loss, ICW decreases while ECW increases [24, 25]. Various mechanisms have been proposed to explain the decline in ICW following weight loss. It is estimated that for every gram of glycogen, approximately 2.7–4 g of water are stored alongside it [26]. Consequently, a reduction in glycogen levels within skeletal muscle cells during periods of calorie restriction may lead to a redistribution of water, contributing to a decrease in ICW and an increase in ECW. Another study conducted by Shiose et al. demonstrated that carbohydrate loading, which replenishes glycogen stores in skeletal muscle, leads to an increase in ICW in the lower limbs due to increased glycogen storage [27]. Additionally, factors such as proteolysis and reduced activity of the sodium–potassium ATPase pump, often linked to insulin deficiency, can disrupt intracellular electrolyte–water balance, promoting a shift of water toward the extracellular space [28]. As mentioned earlier, we found a strong association between a reduction in PhA and an increase in ECW/TBW ratio, indicating disruption of cellular membrane integrity and a subsequent shift of water from the intracellular to the extracellular compartment.

After ECW/TBW, the strongest direct correlations were observed for changes in WHR, weight, BFM, BMI, and SMM. Teixeira et al. reported a negative relationship between reductions in PhA and the percentage of weight loss after bariatric surgery ($r = -0.48$, $p < 0.001$) [29]; similarly, our study revealed a direct correlation between weight loss and reductions in PhA. Additionally, this study revealed a statistically significant positive correlation between reductions in PhA and losses of SMM ($r = 0.31$, $p < 0.001$), BFM ($r = 0.28$, $p < 0.001$), and BMI ($r = 0.41$, $p < 0.001$) [29], which aligns with our findings.

Among the main components of body weight (BFM, lean body mass (LBM), and SMM), the strongest association was observed between changes in SMM and PhA. The weakest associations with changes in PhA were found for changes in BFM, BFP, and VFL. These results suggest that changes in BFM have the least effect on PhA, whereas changes in ECW/TBW ratio (inversely) and SMM (directly) have the greatest effect. These results align with the findings of Skrzypek et al., who reported strong positive correlations between LBM and PhA ($r = 0.73$) and between SMM and PhA ($r = 0.79$). In addition, SMM was a significant predictor of PhA in the regression model ($\beta = 0.10$, $p < 0.001$) [30]. Conversely, BFM was inversely associated with PhA in the regression model ($\beta = -0.13$, $p < 0.001$) [30]. This difference may be

attributed to the longitudinal nature of the present study, in which changes in BFM are associated with increase or decrease in the number of cell membranes, affecting reactance levels^[30] and ultimately leading to corresponding changes in PhA.

The present study revealed a significant direct association between changes in weight and changes in PhA. Najafi et al. reported that PhA significantly decreased following a period of weight loss^[23]. In contrast, Hurtado et al. demonstrated that PhA significantly increased after a period of weight gain in individuals with anorexia^[31]. In the study by Papadia et al., which examined an enterally administered ketogenic diet in individuals with overweight and obesity, the percentage of weight change was directly correlated with changes in PhA; however, this association was not statistically significant ($\beta = 0.67$, $p = 0.47$)^[32]. After adjusting for WC and BFM in the regression model, this association became inverse and statistically significant ($\beta = -1.34$, $p = 0.006$). In contrast, in Model 2 of our study, in which the effects of changes in ECW/TBW and WHR were adjusted for, the association remained direct and significant. The inclusion of BFM and SMM in the linear mixed-effects model resulted in multicollinearity, making it impossible to examine these variables, which could potentially alter the association.

The linear mixed-effects model showed that the association between weight changes and PhA changes was significantly stronger in women than in men. This indicates that the same amount of weight change results, on average, in greater changes in PhA among women. Previous studies have reported that men generally have higher PhA values than women^[3, 13, 30], which is thought to be attributable to their higher lean mass^[33]. It is assumed that the smaller changes in PhA observed in men are related to the protective effect of their greater lean mass and SMM.

Statistical analysis showed that changes in PhA were significantly associated with weight changes in both age groups, with a stronger association in the older adults, indicating that they experience greater changes in PhA per unit of weight change than adults under 60. A German study by Bosy-Westphal et al. conducted in a population of young adults reported that sex and age were the main determinants of PhA, with higher values observed in men and in younger individuals^[13]. Additionally, several studies have shown that PhA values decrease with age^[8, 34, 35]. The primary reason for this decline is the age-related reduction in cellular body mass and the increase in extracellular volume, leading to a higher ECW/ICW ratio^[8]. Furthermore, both muscle mass and muscle strength decrease with age; however, the decline in muscle strength is considerably greater than the reduction in muscle mass^[36]. Given that cellular body mass and muscle mass, which have the greatest influence on PhA, are lower in older adults^[37], greater muscle mass at younger ages may mitigate changes in PhA. As individuals age and these factors decline, weight changes may have a more substantial effect on changes in PhA.

The results based on BMI classification showed that weight changes had the smallest effect on PhA in individuals with obesity and the largest effect in those with underweight. Higher BMI was associated with smaller changes in PhA, possibly due to obesity-related factors such as inflammation, oxidative stress, and mitochondrial dysfunction, which can negatively affect cellular health^[38]. This may ultimately

lead to differences in the impact of weight changes on PhA across BMI categories. Moreover, the higher estimate observed in individuals with underweight compared to those with obesity suggests that individuals with underweight may experience increases in PhA—and consequently improvements in cellular health—with weight gain up to the overweight category, after which the magnitude of the estimate decreases. From a clinical perspective, this may be interpreted as physiological regulatory response that moderates the direct longitudinal association between increases in PhA and body weight under conditions of excessive weight gain.

Individuals with obesity are generally recommended to lose weight in order to benefit from the positive health effects of weight reduction. However, weight loss can lead to decreases in PhA, a marker of cellular health. For this reason, weight management strategies should aim to reduce body weight while minimizing declines in PhA to preserve optimal cellular function. This objective can be achieved by reducing body fat while increasing or maintaining muscle mass.

The results of our study showed a positive and significant association between weight changes and PhA changes in both individuals who used body-contouring devices and those who did not; however, the difference in the estimates between the two groups was not statistically significant. Because body-contouring devices primarily target localized fat cells ^[39], and given the findings in Table 2 indicating that BFM had a relatively smaller effect on PhA changes, the minimal difference observed between the two groups is likely attributable to this factor.

The association between weight changes and PhA changes appeared to weaken over longer time intervals. The strongest relationship was observed during the 0–3 months interval, whereas the 0–12 months interval yielded a statistically significantly smaller estimate. These findings suggest a potential plateau effect on PhA responsiveness to weight changes over time, which may be attributed to metabolic adaptations that occur with prolonged weight change ^[17].

The analysis of linear mixed models demonstrated a direct and significant relationship between weight changes and PhA changes in both the weigh-gain and weight-loss groups, with changes in PhA being statistically greater among individuals who gained weight. These findings suggest that the body attempt to maintain and protect its cellular health during weight fluctuations. During weight loss, the body appears to resist substantial declines in PhA, whereas during weight gain, it more readily facilitates increases in PhA.

This study had some limitations. Potential confounding factors, such as physical activity levels, dietary intake, hydration status, and medication use were not controlled for, which may influence the observed associations. Although bioimpedance analysis was performed according to standardized protocols, the method remains sensitive to factors such as hydration and time of day, which could introduce measurement variability. Despite these limitations, the study also possesses several notable strengths. The inclusion of more than 6,000 participants provided substantial statistical power to detect meaningful associations between changes in PhA and changes in weight and body composition. The

longitudinal design, with a one-year follow-up period, enabled the assessment of dynamic temporal changes in PhA, offering insight into its responsiveness over time. Furthermore, stratification of the analyses by demographic and clinical factors—including age, sex, BMI categories, and intervention type—enhanced the interpretability of the findings and allowed for a more nuanced understanding of variability in PhA responses.

Conclusion

This study demonstrated a positive and significant association between changes in PhA and alterations in body weight across diverse demographic and clinical groups. The responsiveness of PhA was influenced by age, BMI, sex, intervention type, and time interval, with older adults and individuals with underweight exhibiting greater sensitivity. These findings highlight the potential utility of PhA as a biomarker for monitoring cellular health and body composition during weight management interventions. Further research is warranted to elucidate the mechanisms underlying PhA changes and to clarify their implications for personalized nutrition and clinical practice.

Declarations

Competing Interests:

The authors have no competing interests to declare that are relevant to the content of this article.

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Author Contribution

AED, NS, and MGM conceived the study and designed the methodology. AED, HE, RS, NAG, NA, and MAM contributed to data collection. AED and MN drafted the original manuscript. AED and HE performed the formal analysis, and MA contributed to the methodology. GAF and NS contributed to revising the manuscript. NS and MGM supervised the study. All authors critically reviewed the manuscript and approved the final version.

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Data Availability

The datasets analysed during the current study are available from the corresponding author on reasonable request.

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Figures

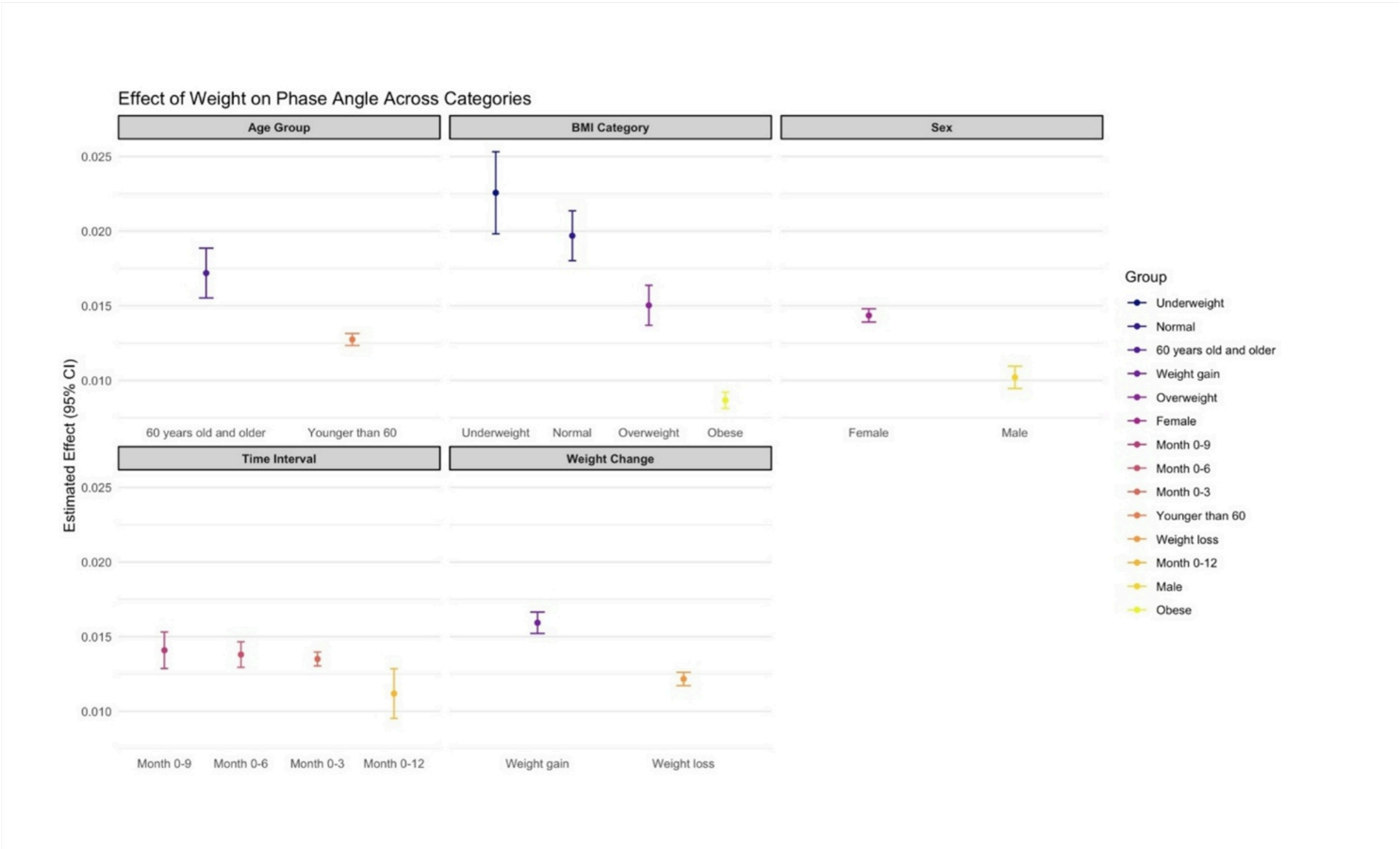


Figure 1

Summary of the longitudinal association of phase angle with weight among all study groups