Nutrition 61 (2019) 70–76

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

# Smoking status affects bioimpedance-derived phase angle in men but not in women: The Pró-Saúde Study, Brazil

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ARTICLE INFO

*Article History:*
Received 27 July 2018
Received in revised form 18 September 2018
Accepted 23 October 2018

*Keywords:*
Bioelectrical impedance
Phase angle
Cellular integrity
Inflammation
Smoking status

ABSTRACT

*Objective:* Phase angle (PhA) is determined by bioelectrical impedance (BIA) and it is interpreted as an index of cell membrane integrity. Smokers are susceptible to systemic oxidative stress and often adopt unhealthy habits, which may contribute to cellular damage. This unfavorable conjuncture may result in lower PhA in smokers. The aim of this study was to investigate the association between PhA and smoking status.
*Methods:* This cross-sectional study included 247 (48%) adult men. Body composition and PhA were determined using dual-energy x-ray absorptiometry and BIA, respectively. Blood sampling, food habits, and smoking status information were collected. Statistical analyses were performed for each sex separately. Analysis of covariance controlling for body mass index and age compared PhA values across smoking categories. Multiple linear regression determined whether smoking status was a PhA predictor.
*Results:* PhA was lower in male current smokers (6.6 ± 0.13°) compared with never-smokers (7 ± 0.06°; $P = 0.038$). The ratio of extracellular to intracellular water was higher in current ($P = 0.003$) and former male smokers ($P = 0.006$) compared with never-smokers. Body composition did not differ in male and female smoking categories. Male current smokers ingested more calories, protein, carbohydrates, and alcohol than never and former smokers ($P < 0.05$). Current female smokers had higher alcohol consumption compared with never smokers ($P = 0.019$). Male current smokers presented lower than never-smokers (unstandardized β coefficient = −0.202; 95% confidence interval, −0.359 to −0.046). Smoking status was associated with PhA decrease only in men.
*Conclusion:* The results from the present study suggest that being a current smoker results in lower PhA in men, even when controlling for other variables.



## Introduction

Cigarette smoking is a major cause of preventable disease and premature death around the world, with most of these deaths occurring in low- and middle-income countries [1]. This conjuncture may be worse considering that, in general, smokers tend to adopt other unhealthy habits, including consumption of fewer nutritious foods, larger amounts of alcoholic beverages, more calories [2], and a sedentary lifestyle that, ultimately, may affect body composition [3]. Smoking results in muscle wasting owing to cigarette smoke substances that stimulate proteolysis and impair protein synthesis. In addition, proinflammatory cytokines may contribute to smoking-induced muscle loss [4]. It is well established that cigarette smoking is an abundant source of prooxidant substances; it decreases antioxidant defenses and leads to inflammatory response characterized by elevated C-reactive protein (CRP) and other inflammatory markers [5]. Adverse effects of cigarette smoking on lung health and other organ systems are

This study was financed in part by the Coordenação de Aperfeiçoamento de Nível Superior – Brasil (CAPES) – Finance code 001 and Fundação de Amparo à Pesquisa do estado do Rio de Janeiro - FAPERJ (grant no. E-26/110.119/2013). All authors participated in the conception and design of the study; data collection; analysis and data interpretation; drafting or revision; and approval of final manuscript. The authors have no conflicts of interest to declare.

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https://doi.org/10.1016/j.nut.2018.10.029
0899-9007/

linked to exposure to inflammatory mediators and oxidative stress, leading to damage of biomolecules including fatty acids in cell membranes [6].

Important cellular characteristics like membrane integrity, permeability, water distribution between intra- and extracellular spaces, and quantity of cells can be assessed by bioelectrical phase angle (PhA) [7]. PhA is a raw variable derived from bioelectrical impedance and age, sex, body mass index (BMI), fat-free mass (FFM), and fluid distribution are major PhA predictors in healthy individuals [8–11]. Higher PhA values are indicative of more intact cell membranes and body cell mass, whereas smaller values suggest cell death or decreased cell integrity and function [12].

Inflammation is a significant determinant of PhA decrease in disease [13]. Recently, it was demonstrated that PhA presented an inverse association with interleukin (IL)-6, tumor necrosis factor-α, and CRP and it was directly associated with catalase and total radical-trapping antioxidant [14]. In addition to inflammation, malnutrition or disease-specific parameters are also associated with decreases in PhA, which explains its relevant role as a prognostic indicator in different clinical conditions [13]. Studies have shown PhA predictive potential in solid or hematologic tumor diseases [15] and in clinical outcome in patients on maintenance hemodialysis [16]. Patients with lower PhA had impaired muscle function, decreased quality of life, and increased morbidity and mortality. In chronic heart failure, lower PhA values were associated with malnutrition and worsening of heart failure symptoms [17]. Regarding smoking-related diseases, in patients with non-small cell lung cancer, PhA was a predictor of survival [18] and it was inversely associated with tumor volume [19].

Systemic oxidative stress and inflammation caused by smoking per se, in addition to consequences of an unhealthy lifestyle often adopted by current smokers, may result in lower PhA values. Although smoking is a common behavior, its effects on PhA have not been evaluated to our knowledge. The knowledge about PhA predictors is necessary for the appropriate use of PhA as an indicator of nutritional status and prognosis in different clinical conditions. It seems relevant to consider that biological variables may not be the only ones to affect PhA. Therefore, the main purpose of the present study was to investigate the association between PhA values and smoking status.

## Methods

### *Study design and participants*

This cross-sectional study was nested within the Pró-Saúde Study (EPS). The EPS is a prospective cohort study of non-faculty civil public servants at the Rio de Janeiro State University, Brazil, focusing on investigation of health-related social and behavioral determinants [20]. Four phases of data collection were conducted among 3253 participants (1999, 2001, 2006, and 2012). During the fourth data collection phase, a subgroup of 520 participants (270 women and 250 men) were randomly selected within age, sex, and schooling strata to perform body composition analysis by dual-energy x-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), anthropometric evaluation, and blood sampling and to collect information on dietary habits and social and behavioral characteristics. Data collection was carried out between July 2012 and October 2013. Three participants were excluded from the analysis because of PhA values <4°. These values were considered extreme outliers, representing possible measurement error, after exclusion of any condition that would explain those values (e.g. advanced age and impairment of nutritional status). Two participants with missing information related to smoking habits were excluded from study. Final analysis included 247 men and 268 women.

This study was approved by the Ethics in Research Committee of the Institute of Social Medicine at the State University of Rio de Janeiro. All participants signed an informed consent form.

### *DXA*

Fat mass (FM) and FFM were measured by DXA (iDXA Lunar equipment, GE Healthcare, Madison, WI, USA). Participants were told to wear light clothing without metal accessories. They were placed in dorsal recumbent position and asked to remain motionless until the end of the procedure [21]. All scans were performed by the same trained professional, and equipment was calibrated daily according to manufacturer's protocol. Measurements of the manufacturer-supplied calibration block (daily) and column calibration block (weekly) showed a <0.7% coefficient of variation [21]. FFM and FM were expressed in kilograms (kg).

### *BIA*

BIA was conducted using a BIA 450 Bioimpedance Analyzer (Byodynamics Corp., Shoreline, WA, USA), which applies an alternating current of 800 μA at a single frequency of 50 kHz. Whole body BIA measurements were taken between the right wrist and ankle, with the participant in supine position, in a thermo-neutral environment of 25°C. To avoid disturbances in fluid distribution, participants were instructed to abstain from foods and liquids for at least 4 h, not to drink alcohol during 48 d, and to refrain from caffeine intake and intense physical activity 24 h before BIA. Women were requested not to perform the exam during menstrual period [22]. Before each testing session, the analyzer was checked with a calibration circuit of known impedance (resistance = 500 ohms; reactance = 0.1 ohms, 0.9% error).

Whole body impedance consists of two components: resistance (R), the opposition to alternating electric current flow exerted by intracellular and extracellular ionic solutions, and reactance (Xc), defined as a delay in conduction of the applied current exerted by cell membranes and tissue interfaces [23]. R and Xc were used to calculate PhA values by the following equation [23]:

$$\mathrm{PhA}(^{\circ}) = \text{arc tangent}(\mathrm{Xc}/\mathrm{R}) \times (180^{\circ}/\pi)$$

Total body water (TBW, L) was calculated using single-frequency BIA. According to the manufacturer, the equation was based on Kushner and Schoeller [24], in which deuterium dilution was used as a control method to measure TBW. Intracellular water (ICW, L) equation was based on the relationship between body cell mass and ICW, described by Cohn et al [25]. Extracellular water (ECW, L) = TBW − ICW. ECW and ICW compartments were used to calculate the ECW-to-ICW ratio.

### *Inflammation marker*

Serum samples were collected and high-sensitivity C-reactive protein (hs-CRP, mg/dL) was measured with a turbidimetric immunoassay and performed according to manufacturer instructions (BioSystems S.A., Barcelona, Spain).

### *Anthropometric data*

Height in meters (m) was measured with a fixed stadiometer and weight in kilograms (kg) determined with a digital scale. Anthropometric measurements were determined according to standardized procedures [26]. BMI was calculated from the ratio between weight and the square of the height. The cutoff points used to classify BMI (kg/m$^2$) were those proposed by the World Health Organization (WHO) [27].

### *Dietary intake assessment*

A food frequency questionnaire (FFQ) previously validated [28] for Brazilian population was used to obtain dietary information. Participants were requested to indicate frequency and portion size of food and alcohol beverage consumed, which allowed average daily amount over the past 6 mo to be quantified. Nutrient intake information, including alcohol, calorie, protein, carbohydrates, and fat was calculated using the US Department of Agriculture (USDA) food composition databases [29].

### *Demographic variables and smoking status*

Demographic information such as age and sex were collected. Self-related information on smoking status was obtained from the question "Do you currently smoke cigarettes?" and the following response options: “Yes”; “No, I have never smoked”; “No, I quit smoking 1 y (or more) ago”; or “No, I quit smoking less than 1 y ago.” Participants who have never smoked were categorized as never-smokers, those who quit smoking were categorized as former smokers, and those who responded positively were referred to as current smokers.

### *Statistical analysis*

All analyses were performed separately for each sex and participants were classified according to smoking status. Continuous variables were expressed as means ± standard deviation. Smoking group differences in age, hs-CRP levels, anthropometric, body composition, and dietary intake data were tested with one-way analysis of variance (ANOVA). Because in previous studies age and BMI were considered major PhA predictors [8–10], analysis of covariance (ANCOVA)

controlling for BMI and age was performed to evaluate PhA means across smoking categories. Bonferroni post hoc test was used to perform pairwise comparisons between group means.

A multiple linear regression model assessed the relation between PhA (outcome) and smoking status (exposure) separately for each sex. Additional PhA determinants (ECW:ICW, FFM, CRP) [11,13] were included in regression models as adjustment variables along with BMI and age. Two dummy variables were created (former smokers and current smokers) and never-smokers were considered as the reference group. Regression results were presented as unstandardized b coefficients, 95% confidence intervals (CI) and *P*-value. Significance level was set at 5% and $P < 0.05$ was considered statistically significant. Analyses were conducted with SPSS version 17.0.1. (SPSS, Chicago, IL, USA).

## Results

The most frequent smoking status informed by male (63%, n = 156) and female (63%, n = 169) participants was "never-smokers." Information regarding age, anthropometry, BIA and DXA measurements, hs-CRP levels, and dietary intake between smoking categories in men and women are summarized in Tables 1 and 2, respectively.

Male current and former smokers were older than never-smokers ($P < 0.001$). There were no significant differences in weight, height, and BMI between male smoking categories. Overweight (42.5%) and obesity (30%) were highly frequent among men, with mean BMI being consistent with overweight in all smoking status groups. No differences were found between smoking categories concerning TBW ($P = 0.384$). ECW-to-ICW was higher in male current ($P = 0.003$) and former ($P = 0.006$) smokers than in never-smokers. FM and FFM did not differ between male smoking categories. Serum hs-CRP levels were higher in current smokers than in never-smokers ($P = 0.031$). No significant differences in hs-CRP levels were observed between former and never-smokers. Male current smokers had higher daily calorie, protein, carbohydrate, and alcohol intakes than never- and former smokers ($P < 0.05$). Male former smokers also had higher alcohol intake than never-smokers ($P = 0.032$).

Considering female participants, former smokers were older than never-smokers ($P = 0.022$). Similar to the observed in men, overweight (41.5%) and obesity (29.5%) were highly frequent among women, with mean BMI being consistent with overweight in all smoking statuses. There were no significant differences in TBW, ECW-to-ICW, FM, FFM, and hs-CRP levels between female smoking categories. Mean daily intake of calories, protein, carbohydrates, and total fat did not differ between smoking categories in women. Female current and former smokers had higher alcohol consumption than never-smokers (current versus never-smokers: $P = 0.019$; former versus never-smokers: $P = 0.031$) and no difference was found between current and former smokers ($P = 0.913$)

Figure 1 shows mean PhA values in male and female smoking categories with age and BMI as covariates. PhA was lower in male current smokers (6.6° ± 0.13°) than in never-smokers (7° ± 0.06°; $P = 0.038$). No differences were found in mean PhA values between male current and former smokers (6.8° ± 0.09°) or between male former smokers and never-smokers (current versus former smokers: $P = 0.504$; former versus never-smokers: $P = 0.578$). PhA means between female never smokers (6° ± 0.05°), former smokers (6.1° ± 0.08°) and current smokers (5.9° ± 0.14°) did not differ ($P = 0.481$).

A multiple linear regression analysis was carried out to identify whether smoking status affects PhA values in men and women (Table 3). The following set of adjustment variables was used: age, BMI, ECW-to-ICW, FFM, and hs-CRP. Current smoking status was a determinant of PhA decrease in men. Male current smokers had PhA 0.2° lower than never-smokers (β = −0.202; 95% confidence interval [CI], −0.359 to −0.046). Smoking status was not associated with PhA variation in women. Adjusted $R^2$ explained about 78% and 96% of PhA variability among men and women, respectively.

## Discussion

In the present study, we sought to investigate PhA values between smoking status in men and women. The results suggest that being a current smoker results in lower PhA in men but not in women. Moreover, smoking status appeared to contribute to PhA

**Table 1**
General characteristics according to male smoking status

| | Men (N = 247) | | | |
|---|---|---|---|---|
| Characteristics | Never-smokersn = 156 | Former smokersn = 59 | Current smokersn = 32 | *P*-value* |
| Age, y†,‡ | 48.5 ± 7.1 | 55.6 ± 7.5 | 56.9 ± 6 | <0.001 |
| Anthropometry | | | | |
| Weight, kg | 81.2 ± 14.3 | 85.9 ± 17.4 | 80.8 ± 13.7 | 0.106 |
| Height, m | 1.72 ± 0.06 | 1.72 ± 0.07 | 1.71 ± 0.07 | 0.824 |
| BMI, kg/m$^2$ | 27.3 ± 4.4 | 28.7 ± 4.9 | 27.4 ± 4.5 | 0.101 |
| BIA | | | | |
| TBW, L | 44.01 ± 6.83 | 45.29 ± 7.57 | 43.42 ± 6.79 | 0.384 |
| ECW:ICW†,‡ | 0.74 ± 0.09 | 0.78 ± 0.09 | 0.80 ± 0.07 | <0.001 |
| DXA | | | | |
| FM, kg | 24.9 ± 8.7 | 28.1 ± 10.5 | 25.0 ± 8.4 | 0.062 |
| FFM, kg | 56.3 ± 7.2 | 57.6 ± 8.6 | 55.6 ± 6.8 | 0.421 |
| hs-CRP, mg/dL† | 0.31 ± 0.63 | 0.37 ± 0.58 | 0.62 ± 0.52 | 0.037 |
| Dietary intake | | | | |
| Calories, kcal/d†,§ | 2774 ± 998 | 2888 ± 1315 | 3621 ± 1848 | 0.002 |
| Alcohol, g/d†,‡,§ | 5.2 ± 7.8 | 9.5 ± 11.7 | 17.1 ± 19.6 | <0.001 |
| Protein, g/d†,§ | 130 ± 50 | 127 ± 56 | 158 ± 84 | 0.027 |
| Carbohydrate, g/d†,§§ | 389 ± 151 | 403 ± 197 | 509 ± 258 | 0.003 |
| Total fat, g/d | 98 ± 39 | 99 ± 50 | 120 ± 79 | 0.054 |

BMI, body mass index; BIA, bioimpedance analysis; DXA, dual-energy x-ray absorptiometry; ECW:ICW, extracellular to intracellular water ratio; FFM, fat-free mass; FM, fat mass; hs-CRP, high-sensitivity C-reactive protein; TBW, total body water
Values shown as mean ± standard deviation
*P-value determined by analysis of variance.
†Bonferroni post hoc test: Significant differences between never-smokers and current smokers.
‡Bonferroni post hoc test: Significant differences between never-smokers and former smokers.
§Bonferroni post hoc test: Significant differences between current smokers and former smokers.

**Table 2**
General characteristics according to female smoking status

| Characteristics | Women (N = 268) | | | |
|---|---|---|---|---|
| | Never-smokersn = 169 | Former smokersn = 75 | Current smokersn = 24 | *P*-value* |
| Age (y) | 51.2 ± 8.9 | 54.1± 5.8 | 52.6 ± 5.8 | 0.026 |
| Anthropometry | | | | |
| Weight, kg | 70.9 ± 13.7 | 74.5 ± 15.9 | 68.5 ± 13.6 | 0.101 |
| Height, m | 1.60 ± 0.06 | 1.59 ± 0.07 | 1.61 ± 0.07 | 0.597 |
| BMI, kg/m$^2$ | 27.8 ± 5.1 | 29.3 ± 5.7 | 26.4 ± 5 | 0.035 |
| BIA | | | | |
| TBW, L | 32.72 ± 4.44 | 33.34 ± 4.70 | 31.80 ± 4.39 | 0.317 |
| ECW:ICW | 0.98 ± 0.10 | 1.00 ± 0.13 | 0.99 ± 0.11 | 0.301 |
| DXA | | | | |
| FM, kg | 29.7 ± 9.1 | 32.6 ± 11.23 | 28.4 ± 9.6 | 0.058 |
| FFM, kg | 40.9 ± 5.7 | 41.7 ± 5.6 | 40.6 ± 5.8 | 0.450 |
| hs-CRP, mg/dL | 0.39 ± 0.56 | 0.54 ± 0.73 | 0.38 ± 0.3 3 | 0.163 |
| Dietary intake | | | | |
| Calories, kcal/d | 2299 ± 893 | 2445 ± 810 | 2199 ± 877 | 0.356 |
| Alcohol, g/d†,‡ | 2.9 ± 5.4 | 5.4 ± 9.9 | 7.1 ± 6.5 | 0.003 |
| Protein, g/d | 108 ± 44 | 112 ± 44 | 105 ± 42 | 0.645 |
| Carbohydrate, g/d | 336 ± 149 | 347 ± 127 | 302 ± 145 | 0.410 |
| Total fat, g/d | 82 ± 33 | 87 ± 32 | 79 ± 33 | 0.492 |

BIA, bioimpedance analysis; BMI, body mass index; DXA, dual-energy x-ray absorptiometry; ECW:ICW, extracellular to intracellular water ratio; FFM, fat-free mass; FM, fat mass; hs-CRP, high-sensitivity C-reactive protein; TBW, total body water
Values are shown as means ± SD
*$P$-value determined by analysis of variance.
†Bonferroni post hoc test: Significant differences between never-smokers and current smokers.
‡Bonferroni post hoc test: Significant differences between never-smokers and former smokers.

variation in men, even if other PhA predictors were considered. To our knowledge, this was the first study to investigate whether smoking status has an influence on PhA values in men and women.

Previous studies have shown that, in addition to sex, BMI and age were major PhA predictors in healthy individuals [8–10]. PhA decreases with advancing age owing to a reduction in Xc associated with loss of muscle mass and owing to higher R related to increasing FM [7]. Apart from this, increases in PhA values associated with higher BMI reflect increased number of muscle and fat cells [7]. The present results demonstrated that male current smokers had lower PhA values, regardless of age or BMI influences. Data related to body composition, inflammation, and dietary habits, in particular alcohol intake, may help to elucidate the differences found in PhA values between male smoking categories.

It has been shown that ECW-to-ICW has an inverse association with PhA and it was considered as a determinant of this bioelectrical index [11]. A higher ECW-to-ICW ratio may result from loss of skeletal muscle and enlargement of adipose tissue, which is a typical age-related body composition change [7], or it could be a reflection of clinical status in patients with acute or chronic diseases [30]. In the present study, male smokers had higher ECW-to-ICW than never-smokers. Similar to current smokers, former smokers also had higher ECW-to-ICW than never-smokers, which suggested smoking cessation may not be associated with full recovery of cell membrane structure and functionality. There were no differences in BMI, and neither FM nor FFM measured by DXA differed between male smoking categories. These results showed that even in situations where loss of muscle mass or an increase in FM has not occurred, ECW-to-ICW may be affected.

Smoking is associated with systemic inflammation and increased levels of proinflammatory cytokines, including CRP [5,31]. Male current smokers had higher hs-CRP levels than never-smokers in the present analysis. This finding is in agreement with previous studies in which current smokers were more susceptible to chronic low-grade inflammation, with CRP levels significantly higher than never-smokers [32–34]. After smoking cessation, it was demonstrated that CRP decreases to levels compared with never-smokers, although the timing for this reduction to occur was controversial [34,35]. In a cross-sectional study with ELSA-Brasil participants, CRP in former smokers returned to similar levels to never-smokers after 1 y of smoking cessation [36]. Timing of smoking cessation was not considered in the present analysis, but the results showed that male former smokers had hs-CRP levels similar to male never-smokers, which may represent a decrease in inflammatory response. Relationship between smoking and inflammation has been widely established. The effects of inflammatory markers on PhA values have been demonstrated as well. Inflammation was identified as a predictor of PhA decreases in disease [13]. In patients on hemodialysis, an inverse association between PhA and IL-6 levels was observed regardless of FM and ECW [37]. In the present study, in addition to higher CRP levels, current male smokers had lower PhA values than never-smokers. This finding suggests a possible link between smoking and inflammation and, consequently, decreases in cellular integrity.

Nutrient intakes of smokers usually differ from never-smokers and an unhealthier dietary pattern is common among current smokers [2]. Although smoking is associated with appetite suppression [38], in the present study, total calorie, protein, and carbohydrate intakes were higher in male current smokers than in never-smokers and former smokers. Although not statistically significant, there was a trend of higher total fat consumption among male current smokers. In contrast to the present findings, a study with smokers and non-smokers reported lower energy intake in smokers and no differences were found in protein, fat, carbohydrate, and alcohol ingestion [39]. A meta-analysis of patterns of nutrient ingestion between smoking categories found that smokers had higher intakes of energy and total fat but did not differ from nonsmokers in relation to protein and carbohydrate. Moreover, differences between current and never-smokers were particularly important regarding alcohol consumption, which was higher in current smoker groups in all publications included in this review [2]. The present results showed male current smokers drank greater amounts of alcohol than did male never-smokers and former smokers. Daily alcohol consumption was also significantly higher in former smokers than in never-smokers.

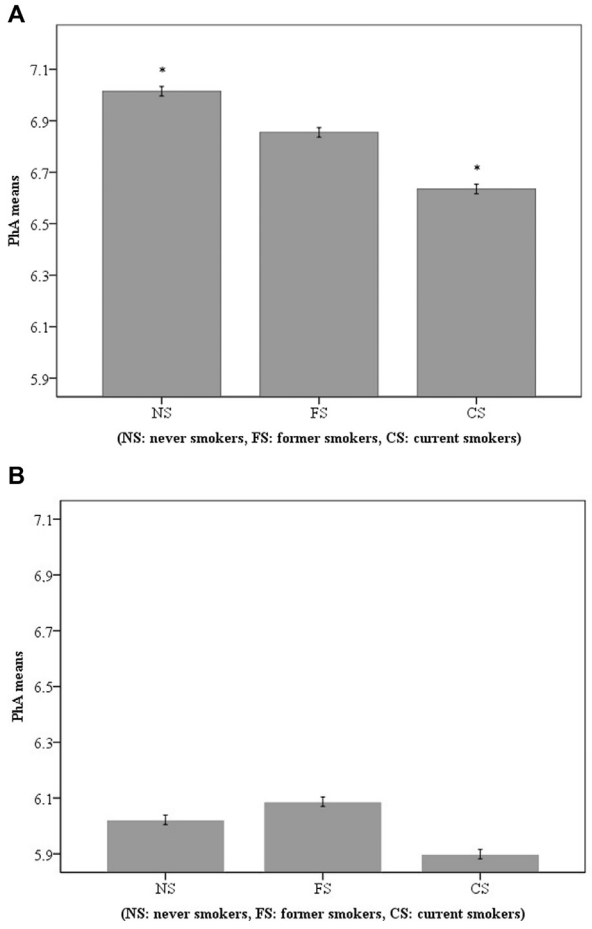


**Fig. 1.** Differences in mean PhA values in male (**A**) and female (**B**) smoking status with body mass index and age as covariates. Analysis of variance controlling for body mass index and age means and Bonferroni post hoc test. PhA values in degrees (°). *Statistically significant difference ($P < 0.05$). CS, current smoker; FS, former smoker; NS, never-smoker; PhA, phase angle.

Ethanol metabolism leads to an environment favorable to oxidative stress, modification of biological structures and, consequently, results in malfunction of cells and tissues [40]. Hence, this significantly higher alcohol intake in male current smokers could be considered an additional factor to deleterious effects of smoking on cellular health.

In addition to lower PhA in male current smokers, it was observed that current smokers status was a determinant of PhA in men. Multivariate regression modeling controlling for age, BMI, ECW-to-ICW, FFM, and hs-CRP showed current smokers had PhA values lower than never-smokers and this predictor model explained about 78% of PhA variability in men. Associations of PhA with sex, age, and BMI have been well established in large studies in different populations [8–10]. Recently, FFM and height [11] were identified as additional PhA predictors and even ethnicity [41] was considered as a variable that should be accounted for when determining population reference PhA values. The present results demonstrated that current smoker status, a common behavioral variable, was a predictor of PhA decreases in men. Therefore, smoking status also should be considered as an adjustment variable in future studies, particularly among men.

Body composition variables measured by DXA did not differ between female smoking categories. This similarity in body weight, FM, and FFM was not expected in either female or male smoking groups. Nicotine has many effects on regulation of eating and energy expenditure and a lower body weight is expected among smokers because of its anorectic effects and increases in metabolic rate. On the other hand, it is common for former smokers to gain weight after smoking cessation, corresponding mainly to increases in FM. Mechanisms of weight gain after smoking cessation include decreased metabolic rate and increased caloric intake, opposite effects to those produced by nicotine [38] Although alcohol intake was higher in female current and former smokers, total daily calorie intake did not differ between smoking categories in the present analysis. Therefore, the findings on nutrient intake explain the similarities found in body composition between female smoking categories.

Serum hs-CRP levels did not differ between female smoking categories in the present study. It has been shown that CRP levels increase as a consequence of hormone replacement therapy (HRT) [42,43], and considering mean age of women included in the present study, it seems appropriate to consider a possible influence of hormone replacement therapy on this inflammatory marker. Somewhat surprisingly, PhA values did not differ between female smoking categories. In addition to this finding, current status was not a PhA determinant in women. The Global Adult Tobacco Survey, a household-based survey designed to obtain information about tobacco use behavior in low- and middle-income countries, including Brazil, showed that prevalence of tobacco smoking was generally much higher for men than women. In addition, average age of smoking initiation was older in women than in men and mean number of cigarettes smoked per day higher among male smokers [44]. The similarity in PhA values between female smoking categories may possibly be explained by a different smoking behavior. It is possible that women were less exposed to toxic

**Table 3**
Association between PhA and smoking status in male (n = 247) and female (n = 268) participants

| | Men* | | | Women† | | |
|---|---|---|---|---|---|---|
| Variables | β | 95% CI | *P*-value | β | 95% CI | *P*-value |
| Former smokers‡ | −0.086 | −0.211 to 0.039 | 0.176 | 0.035 | −0.006 to 0.076 | 0.090 |
| Current smokers‡ | −0.202 | −0.359 to −0.046 | 0.012 | −0.024 | −0.087 to 0.039 | 0.447 |
| Age, y | 0.003 | −0.004 to 0.010 | 0.394 | 0.019 | 0.016 to 0.022 | <0.001 |
| BMI, kg/m$^2$ | 0.039 | 0.024 to 0.053 | <0.001 | 0.036 | 0.030 to 0.041 | <0.001 |
| ECW:ICW | −7.035 | −7.580 to −6.491 | <0.001 | −7,190 | −7.386 to −6.993 | <0.001 |
| FFM, kg | 0.019 | 0.010 to 0.028 | <0.001 | 0.045 | 0.040 to 0.049 | <0.001 |
| hs-CRP, mg/dL | 0.003 | −0.078 to 0.084 | 0.941 | −0.018 | −0.052 to 0.016 | 0.306 |

BMI, body mass index; ECW:ICW, extracellular to intracellular water ratio; FFM, fat-free mass; hs-CRP, high-sensitivity C-reactive protein
Multivariate linear regression adjusted for age, BMI, ECW:ICW, FFM, and hs-CRP
*Adjusted $R^2$ 0.778; SE of the estimate = 0.374
†Adjusted $R^2$ 0.957; SE of the estimate = 0.145
‡Never-smokers were considered the reference category.

effects of cigarettes that could lead to cell damage and, ultimately, affect PhA.

Unlike women, current male smokers were more susceptible to cellular damage, which was demonstrated by the identification of lower PhA values than never-smokers. Higher hs-CRP levels and ECW-to-ICW are indicative of inflammation and cellular structure impairment, which could be exacerbated by deleterious effects of a greater daily alcohol intake in male current smokers. In addition, current smoking was identified as a determinant of PhA in men.

Some limitations of the present study should be considered. Unfortunately, the lack of full information on smoking behavior is one of them. Number of cigarettes smoked per day, age at smoking initiation, and duration of smoking [45] would be relevant data to properly explain the unprecedented association between PhA and smoking habits in male participants and also to explain the similarity found in PhA values among female smoking categories. Although ECW and ICW compartments were not determined by gold standard methods, the results were not inaccurate because participants did not have any medical condition in which major disturbances of water distribution were prominent.

## Conclusion

The main finding of the present investigation was to indicate a possible impairment of cellular integrity in male current smokers, even though they are not critically ill or malnourished. The results open up a new window for future research about a possible PhA application as a screening tool to identify, among male current smokers, those at risk of inflammation, cell damage, and diseases caused by smoking. In addition, if application of PhA as indicator of nutritional status and prognosis in different clinical conditions depends on the knowledge about its predictors, it seems relevant to consider the role of smoking status on PhA.

## Acknowledgments

The authors acknowledge the participants of the Pró-Saúde Study and the Interdisciplinary Nutrition Assessment Laboratory of the State University of Rio de Janeiro.

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