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Phase angle as a predictor of muscle mass in patients with inflammatory bowel disease

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HIGHLIGHTS

- This study aims to assess whether the phase angle is a parameter for predicting reduced muscle mass in patients with inflammatory bowel disease.
- There was a correlation of the phase angle with skeletal muscle mass and the associations remained in disease activity.
- The ROC curve analysis indicated that the cut-off point of the PhA ≤5.042° for women and PhA ≤6,079° for men can be used to predict muscle mass reduction.
- The phase angle can be considered a predictor of muscle mass reduction in inflammatory bowel disease.

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ABSTRACT – Malnutrition/sarcopenia is frequent in patients with inflammatory bowel diseases (IBD), and results in muscle catabolism, impacting treatment response, postoperative complications, and quality of life. **Objective** – This study aims to assess whether the phase angle (PhA) is a parameter for predicting reduced muscle mass in patients with IBD. **Methods –** Adult patients with IBD were included in this cross-sectional study. For the estimation of muscle mass and the calculation of the PhA, we used bioelectrical impedance analysis (BIA). Crohn's disease (CD) and ulcerative colitis (UC) activity scores were defined using the Harvey-Bradshaw index and partial Mayo score, respectively. The area under the ROC curve was calculated to identify the PhA cut-off point for reduced muscle mass. **Results –** The sample consisted of 145 patients, with 39 (26.9%) with IBD in the active phase. There was a correlation of the PhA with skeletal muscle mass (SMM) (r_s 0.35, P<0.001) and with the skeletal muscle mass index (SMI) (r_s 0.427, P<0.001), and the associations remained in the most active form (moderate or severe) of IBD. The ROC curve analysis indicated that the cut-offs points of the PhA ≤5.042 for female and PhA ≤6.079 for male can be used to predict muscle mass reduction. **Conclusion –** The PhA can be considered a predictor of muscle mass reduction in IBD patients, and we can use it for screening and monitoring the evolution of malnutrition.

Keywords – Phase angle; malnutrition; inflammatory bowel disease; skeletal muscle mass.

INTRODUCTION

Inflammatory bowel diseases (IBD) mainly consist of Crohn's disease (CD) and ulcerative colitis (UC), both of which are classified as chronic inflammatory diseases and cause digestive disorders and inflammation of the gastrointestinal tract[1,2]. The prevalence of malnutrition is about 75% and 69% in patients with CD and UC, respectively[3]. Factors such as reduced food intake, malabsorption, increased intestinal losses, drug-nutrient interaction, and increased nutritional requirements contribute to malnutrition in IBD[4,5]. Malnutrition has been associated with increased hospitalizations, aggravation of the disease, surgery, and postoperative complications. Early diagnosis of malnutrition allows nutritional intervention, and, consequently, a positive impact on clinical outcomes[6-8].

Important aspects of malnutrition in IBD patients are related to changes in body composition, mainly muscle mass depletion. In a systematic review, reduced muscle mass was observed in 28% of CD patients and 13% of UC patients, compared to control groups[6] as well as in 60% of IBD patients[7], which shows the importance of including body composition analysis in the evaluation of this population.

Bioelectrical impedance analysis (BIA) is a simple, portable, non-invasive method used to assess body composition[8]. The phase angle (PhA) is determined using BIA, from the relationship between the Reactance (Rc: resistive capacitance of cell membranes) and Resistance (R: pure opposition of the biological conductor to electric current), and represents the amount of cell mass and the integrity of cell membranes[9,10].

Several studies have indicated that the PhA can be considered a prognostic indicator of nutritional status superior to traditional ones, in various diseases[11-13], and it can be used as a tool to identify patients at impaired nutritional and functional risk, as well as assessing disease's progression[14,15].

IBD patients are at high risk of malnutrition, resulting in muscle catabolism, with an impact on response to treatments, surgical complications, and quality of life; therefore, screening and monitoring malnourished patients is critical[16]. Therefore, this study aims to assess whether the PhA is a parameter for predicting reduced muscle mass in patients with IBD.

METHODS

Design of the study and population

Cross-sectional study with a sample of 145 IBD patients (CD=91 and UC=54), in follow-up at the IBD outpatient clinic of the *Hospital Universitário Polydoro Ernani de São Thiago* - HU/UFSC/EBSERH (Florianópolis – Santa Catarina, Brazil), from February to October 2021. Patients over 18 years of age who were treated during the study period and agreed to participate in the study were included, while patients unable to undergo BIA, pregnant or postpartum women were excluded. The project was submitted to the Human Subject Research Ethics Committee (CEPSH-UFSC) and approved under CAAE: 39002720.5.0000.0121 and all participants signed the Informed Consent Form.

Demographic, anthropometric and clinical variables

We obtained demographic and clinical characteristics from the medical records. Trained researchers measured body weight and height using a platform scale with a built-in stadiometer (Welmy®), with the subjects wearing light clothing and barefoot. The formula we used to calculate body mass index was: BMI (kg/m²): Weight/Height² (WHO, 2000). Handgrip strength (HGS) was determined using a hand-held hydraulic dynamometer (Saehan®). The patients were comfortably seated with elbows flexed at 90° and were instructed to press the dynamometer with maximum effort. The strength of both hands was measured three times and we considered the highest value. Low muscle strength was defined as <27 kg for men and <16 kg for women[17]. Disease activity was assessed using the Harvey-Bradshaw Index for patients with CD and c-MAYO score for patients with UC[18,19]

Muscle mass and phase angle

Muscle mass and PhA were determined using BIA equipment (Biodynamic- 310 - Biodynamics Corporation, USA) at 50 kHz. The participants were previously instructed to fast for at least 4 hours, wear light clothing, and to empty their bladders and remove all metal objects before the exam. To perform the examination, the patients were positioned on the

stretcher in supine decubitus with the limbs slightly away from the body and the four electrodes placed in standard positions on the dorsum of the right hand and on the right foot. Data as age, height, weight, gender, and ethnicity were registered in the BIA system. PhA values were calculated as PhA = arc tangent Rc/R x 180°/ π; where π pi= 3.1416[8].

To calculate skeletal muscle mass (SMM), we used the impedance analysis equation from Kyle et al.[20]. The skeletal muscle mass index (SMI) was defined as the skeletal muscle mass divided by the height per meter squared. For categorized SMM, values <20 kg for men and <15 kg for women, and for categorized SMI, less than 7 kg/m² in men and 5.5 kg/m² in women indicate reduced muscle mass[17].

Laboratory analyses

We collected blood samples from the participants without the need of prior fasting to assess nutritional and inflammatory biomarkers (serum albumin, hemoglobin, and C-reactive protein), and the blood tests were performed at the Clinical Laboratory Unit of HU/UFSC/EBSERH, following standardized techniques.

Statistical analyses

Continuous variables appear as medians and interquartile ranges, after verification of normality by Shapiro-Wilk test. We used the Kruskal-Wallis test to evaluate the differences between the medians of the variables in the inflammatory disease activity groups and sex, followed by the Conover post-hoc test to evaluate the difference between the groups. For the analysis of the clinical and nutritional variables, we used Spearman's correlation coefficients. The area under the ROC curve was calculated to identify the cut-off point of the PhA for reduced muscle mass, with sensitivity, specificity, positive predictive value, and negative predictive value obtained through the Youden index. We employed logistic regression in the analysis of the variables associated with reduced PhA. In the adjusted analysis, we estimated the adjusted odds ratios, with their respective 95% confidence intervals. The model was adjusted for sex, age and PhA. *P*-values <0.05 were considered statistically significant. We used Medcalc Statistical Software Version 20.218 (Medcalc Software Ltd, Ostend, Belgium, 2023) for the statistical analyses.

RESULTS

As shown in TABLE 1, we observed significant differences between the stages of disease severity regarding the age (*P*=0.027), anthropometric variables, SMM (*P*<0.001), SMI (*P*<0.001), HGS (*P*<0.001), %BF (*P*<0.001), BMI (*P*=0.034), and biochemical variables (Albumin: *P*<0.001; Hb: *P*<0.001; CRP: *P*<0.001).

The area under the ROC curve for the PhA to predict muscle mass reduction, through SMI, was 0.706 (95%IC 0.599–0.799 *P*=0.001), for female (FIGURE 1) and 0.723 (95%IC 0.590–0.833 *P*=0.003) for male (FIGURE 2). Calculating the Youden index, the optimal cut-off point was PhA ≤5.042 for female, with 81.2% sensitivity and 62.0% specificity and positive predictive values were 32.5% (24.8–41.3), and the negative predictive were 93.6% (83.9–97.6). For male, the optimal cut-off point was PhA ≤6.079 with 87.5% sensitivity and 54.7% specificity. The positive predictive and negative predictive values were 42.4% (33.5–51), and 92% (75.3–97.7), respectively.

Correlation between PhA and demographic, anthropometric, and clinical indicators

Considering all patients, regardless of the stages of disease activity and sex, the correlation coefficients of PhA indicators and muscle mass (SMM and SMI): SMM: r_s 0.35, *P*<0.0001; SMI: r_s 0.427, *P*<0.0001 (TABLE 2A) had statistically significant associations. In patients with active disease (mild, moderate, and severe), the PhA was significantly associated with the SMM and SMI, and it remained in the most active (moderate or severe) forms of the disease (TABLE 2B).

Multivariate logistic regression analysis was performed to determine the associations between PhA and SMI. As presented in TABLE 3, after the categorization of SMI, according to cutoff values for each sex, there was association with PhA, where female patients with PhA ≤5.042º and male patients with ≤6.079º, had 12.11 times more chances of having reduced muscle mass.

DISCUSSION

This study revealed that the PhA had a considerable ability to predict muscle mass reduction in IBD

TABLE 1. Comparison of demographic, anthropometric, and biochemical variables in the stages of disease severity.

Variable	Disease activity						P*
	Remission		Mild		Moderate/severe		
	Female	Male	Female	Male	Female	Male	
Age	48.5 (35.0–59.0)	39.5 (27.0–46.5)	40 (29.2–45.7)[1]	32 (21.5–47.0)[1]	46.5 (34.0–63.0)	32 (29.2–37.7)	0.027
SMM	17.0 (15.3–18.4)[2,4-6]	23.3 (21.7–24.9)[1,3,5-6]	16.6(15.5–18.8)[2,4-6]	20.1 (19.7–24.1)[1,3,5]	14.8 (13.2–16.2)[1-3,4,6]	18.7 (16.8–25.85)[1-3,5]	<0.001
SMI	6.6 (6.2–7.1)[2,4-5]	7.7 (7.1–8.3)[1,3,5]	6.5 (5.4–7.6)[2,5]	7.3 (6.6–7.9)[1,5]	5.7 (5.3–6.3)[1-4,6]	6.7 (6.3–8.5)[5]	<0.001
HGS	25.5 (210–30.0)[2,4,5]	50 (41.0–54.0)[1,3,5-6]	24 (20.5–31.0)[2,4-5]	44 (37.5–50.2)[1,3,5-6]	21 (18.0–24.0)[1-4,6]	24 (18.5–41.2)[2,4-5]	<0.001
%BF	36.2 (30.9–39.9)[2-4,6]	25.1 (19.7–28.3)[1,3,5]	30.9 (28.7–34.8)[1-2,4,6]	19.5 (17.1–25.4)[1,3,5]	30.4 (27.6–34.8)[2,4,6]	13.6 (11.2–18.9)[1,3,5]	<0.001
BMI	27.8 (23.4–31.6)[4,6]	25.8 (23.0–28.0)	24.7 (21.9–29.8)	22.9 (19.9–28.2)[1]	23.1 (20.1–29.9)	20.5 (18.1–24.9)[1]	0.034
R	598 (553–659)[2]	529 (475–578.5)[1,3,5]	589 (507.5–715.5)[2]	556 (487–602)[5]	646.5 (588–706)[2,4,6]	554 (455.5–595.5)[5]	<0.001
Xc	61 (52–73)	54 (46.5–64.0)	64 (50.7–72.5)	59 (49.2–63.5)	50 (46.0–65.0)	64 (41.2–69.5)	0.277
PhA	6.0 (5.0–6.1)	6.1 (4.9–7.0)	6.0 (4.9–7.7)	6.1 (4.9–7.0)	5.02 (4.0–5.1)	8.0 (4.0–8.0)	0.277
Alb (g/L)	4.1 (3.8–4.3)[2,5,6]	4.3 (4.0–4.6)[1,3,4-6]	3.8 (3.5–4.1)[2]	3.7 (2.5–4.3)[2]	3.4 (3.1–3.7)[1,2]	3.3 (2.8–3.5)[1,2]	<0.001
Hb (g/L)	12.9 (12.2–13.6)[2]	14.6 (13.8–15.3)[1,3-6]	12.6 (12.1–13.8)[2]	14.2 (11.9–16.2)[2,5-6]	11.3 (9.5–13.2)[2,4]	11.4 (10.9–13.4)[2,4]	<0.001
CRP (mg/L)	4 (1.3–6.0)[5,6]	2.5 (0.8–6.0)[4-6]	5.5 (1.4–15.8)[5]	5.8 (3.0–29.3)[2]	21.3 (10.0–32.5)[1-3]	20.6 (4.6–43.0)[1,2]	<0.001

IQR:Data expressed in median and interquatis intervals; SMM: Skeletal muscle mass; SMI: Skeletal muscle mass index; HGS: Handgrip strength; %BF: Body fat percentage; BMI: Body mass index; R: Resistance; Xc: Reactance; PhA: Phase Angle; Alb: Albumin; Hb: Hemoglobin; CRP:C-reactive protein. *Kruskal-Wallis test.

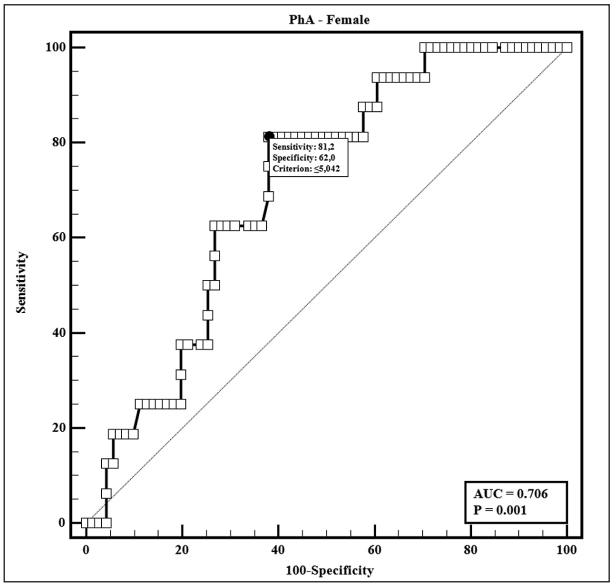

FIGURE 1. ROC curve for evaluation of the phase angle for prediction of muscle mass reduction using skeletal muscle mass index in patients with inflammatory bowel disease, for female patients. PhA: phase angle.

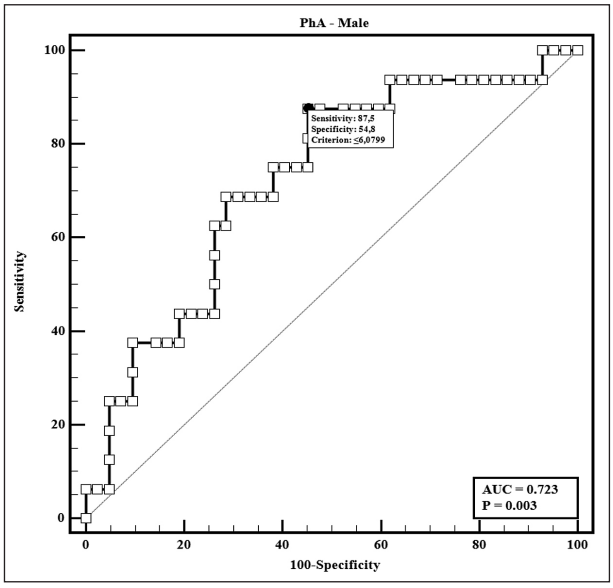

FIGURE 2. ROC curve for evaluation of the phase angle for prediction of muscle mass reduction using skeletal muscle mass index in patients with inflammatory bowel disease, for male patients. PhA: phase angle.

TABLE 2A. Correlation coefficients between PA and individual characteristics, BIA parameters and clinical markers with all disease activity.

n (disease activity)	All		Female		Male	
	n=145 (remission, mild, moderate or severe)		n=85 (remission, mild, moderate or severe)		n=58 (remission, mild, moderate or severe)	
Variables	r_s	*P**	r_s	*P**	r_s	*P**
Age	-0.247	0.0027	-0.192	0.0741	-0.216	0.1028
SMM	0.35	<0.0001	0.326	0.0021	0.487	0.0001
SMI	0.427	<0.0001	0.38	0.0003	0.432	0.0007
HGS	0.127	0.1291	0.071	0.5143	0.12	0.3692
%BF	-0.058	0.4895	0.171	0.1126	-0.17	0.2018
BMI	0.113	0.1755	0.179	0.0976	0.063	0.6363
R	-0.114	0.1739	0.058	0.5961	-0.181	0.1732
Xc	0.781	<0.0001	0.832	<0.0001	0.835	<0.0001
Alb(g/L)	0.096	0.3707	0.065	0.6523	0.01	0.9542
Hb (g/L)	0.126	0.1436	0.118	0.2885	-0.074	0.5996
CRP (mg/L)	0.038	0.6785	0.075	0.5332	0.028	0.85

SMM: Skeletal muscle mass; SMI: Skeletal muscle mass index; HGS: Handgrip strength; %BF: Body fat percentage; BMI: Body mass index; R: Resistance; Xc: Reactance; Alb: Albumin; Hb: Hemoglobin; CRP: C-reactive protein. *Spearman's rank correlation.

TABLE 2B. Correlation coefficients between PA and individual characteristics, BIA parameters and clinical markers with disease activity (mild, moderate and/or severe).

n (disease activity)	All		Female		Male	
	n=39 (mild, moderate and/or severe)		n=25 (moderate and/or severe)		n 14 (severe)	
Variables	r_s	*P**	r_s	*P**	r_s	*P**
Age	-0.121	0.4644	-0.276	0.1821	0.245	0.3985
SMM	0.553	0.0003	0.566	0.0032	0.596	0.0246
SMI	0.651	<0.0001	0.598	0.0016	0.635	0.0147
HGS	0.075	0.6504	0.064	0.7616	0.132	0.6528
%BF	-0.0051	0.7587	0.136	0.5175	0.011	0.9703
BMI	0.266	0.1022	0.417	0.0383	0.143	0.6261
R	-0.379	0.0172	-0.287	0.1636	-0.336	0.2398
Xc	0.725	<0.0001	0.739	<0.0001	0.744	0.0023
Alb(g/L)	0.423	0.0908	0.706	0.0226	0.357	0.4316
Hb (g/L)	0.238	0.1498	0.199	0.3505	0.27	0.3499
CRP (mg/L)	-0.231	0.2027	-0.084	0.7241	-0.364	0.2453

SMM: skeletal muscle mass; SMI: skeletal muscle mass index; HGS: handgrip strength; %BF: body fat percentage; BMI: body mass index; R: Resistance; Xc: Reactance; Alb: Albumin; Hb: Hemoglobin; CRP: C-reactive protein. *Spearman's rank correlation.

TABELA 3. Odds ratios obtained through multivariate analysis of factors associated with skeletal muscle mass index (SMI).

Variable	OR	CI95%	*P*	ORa*	CI95%	*P*
Sex (men)	1.6905	0.7664 to 3.7287	0.1933	1.1287	0.4427 to 2.8775	0.7998
Age (1º quartil)	0.2845	0.09568 to 0.8459	0.0238	0.2541	0.0722 to 0.8946	0.0329
Age (2º quartil)	0.275	0.09267 to 0.8160	0.0200	0.1462	0.0408 to 0.5231	0.0031
Age (3º quartil)	0.1719	0.05060 to 0.5838	0.0048	0.0965	0.0241 to 0.3869	0.001
Categorized PhA for muscle mass reduction	7.8652	2.8209 to 21.9300	0.0001	12.115	3.8422 to 38.2005	<0.0001

PhA: Phase angle; OR: odds Ratio (bruto); Ora*: Odds ratio ajustado; SMI: Skeletal muscle mass index. *Logistic regression analyses after adjusted for sex, age and Phase Angle (PhA).
Adjustment for the factors listed in the table. Model – Dependent Variable = SMI categorized according to cut off points defined for each sex; Method ENTER, Overall Model Fit, Significance level *P*<0.00001 Constant -1.68287 (*P*=0.0027); Hosmer & Lemeshow test, Significance level *P*=0.9414; Area under the ROC curve (AUC) = 0.819 (95%CI 0.747–0.878).

patients, accordingly to the obtained AUC (0.706 for female e 0.723 for men). A similar predictive ability was also corroborated based on the associations of PhA and muscle mass variables (SMM and SMI), in which we verified significant increasing correlation coefficients, according to the progression of disease severity.

The PhA is an indicator of tissue fluid distribution and amount of electrical charge that cell membranes can receive, thus, it can be considered a marker of cell membrane integrity and health[8,21]. Higher PhA values indicate proper cell function and cell membrane integrity[8,11]. Reduced PhA values have been observed in inflammatory processes, malnutrition, and reveal worse prognosis in several chronic diseases[10,22].

In malnutrition, there are chances in water balance, with fluid shifts from the intracellular to extracellular space and reduced body's cell mass, both of which decrease PhA[11,22]. Malnutrition is one of the most important factors associated with a poor prognosis in IBD patients[16,23] and should be diagnosed early and treated appropriately, thus allowing better prognosis, reduced complications and mortality, and improved quality of life[16].

In IBD patients alterations in body's composition, mainly in the proportion of body fat in relation to skeletal muscle mass, can be associated with morbidities, including reduction in muscle strength and physical performance, characteristics of sarcopenia. Reduction in lean mass can be associated with metabolic alteration and increased susceptibility to infections, with impacts in the disease' course, response to treatments, surgical outcomes and quality of life[6,24].

In a study with CD patients, the PhA was reduced in the active phase of the disease compared to remission (mean 6.07±0.92° vs 6.58±0.90°, *P*=0.002), and showed an association with disease severity. PhA was also associated with muscle mass (r=0.443; *P*=0.000) estimated by BIA[25].

In this study, we did not observe any differences in the PhA median when comparing the groups according to IBD activity (TABLE 1), but PhA values decreased substantially in women as the disease became more severe. The results were significant when we analyzed the correlation coefficients of PhA associated with muscle mass indicators (TABLES 2A e 2B).

Hypoalbuminemia, when resulting from an inflammatory process or secondary to malabsorption, is often associated with severe malnutrition and it is related to postoperative complications, although it is not an isolated marker of nutritional status[26]. It is noteworthy that there were significant reductions in the medians of serum albumin according to IBD activity (TABLE 1). Similar results of reduced protein markers in the active phase of the disease have been found in other studies[25,27].

Considering that this study showed that patients who obtained a cut-off point of PhA ≤5.042º for women and PhA ≤6.079º for men were 12.11 more likely to have reduced muscle mass, this result proved to be significant for the diagnosis of changes in body composition, specifically fat-free mass. This has evidence that the PhA is an adequate prediction tool in identifying muscle reduction in IBD patients.

To calculate the PhA, BIA is required, which requires only one equipment, simple training, and is a non-invasive test with quick results. The implementation of PhA in the nutritional assessment of IBD patients complements traditional nutritional screening tools, thus enabling more concrete results for early nutritional intervention decisions, aiming at avoiding disease complications.

This study has some limitations. Once it is a cross-sectional design study, conducted in a single center, it may limit the interpretation of the results in the long term, for which the solution could be conducting multicenter cohort studies involving larger samples. Few inflammatory and micronutrient biochemical analyses were examined, which restricted more consistent associations with the PhA.

CONCLUSION

This study demonstrated that the PhA can be considered a predictor of reduced muscle mass in IBD patients.

Authors' contribution

Bongiolo AM, Dal-Pizzol F, and Pires MMS designed the research; Bongiolo AM, Lazarotto BA and RUPP MLC collected the clinical data; Bongiolo AM, Machado MJ, Pires MMS and Dal-Pizzol F analyzed the data and wrote the paper; Pires MMS and Dal Pizzol F reviewed the manuscript.

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Bongiolo AM, Machado MJ, Lazarotto BA, Rupp MLC, Dal-Pizzol F, Pires MMS. Ângulo de fase como preditor de massa muscular em pacientes com doença inflamatória intestinal. Arq gastroenterol. 2024;61:e23095.

RESUMO – A desnutrição/sarcopenia é frequente em pacientes com doenças inflamatórias intestinais (DII), resultando em catabolismo muscular, com impacto nas respostas aos tratamentos, complicações cirúrgicas e na qualidade de vida. **Objetivo** – Este estudo tem como objetivo, avaliar se o ângulo de fase (AF) é um parâmetro para a predição de redução de massa muscular em pacientes com DII. **Métodos –** Pacientes adultos com DII foram incluídos neste estudo transversal. A estimativa da massa muscular e o cálculo do AF foram realizados a partir do exame de bioimpedância elétrica (BIA). As atividades da doença de Crohn e retocolite ulcerativa foram definidas pelo índice Harvey-Bradshaw e escore parcial de Mayo, respectivamente. A área de curva ROC foi calculada para identificar o ponto de corte do AF para a massa muscular reduzida. **Resultados –** A amostra foi composta por 145 pacientes, sendo 39 (26.9%) com DII em fase ativa. Houve correlação do AF com massa muscular esquelética (MME) (r_s 0.35, P<0.001) e com o índice de massa muscular esquelética (IMME) (r_s 0.427, P<0.001), mantendo-se as associações na forma mais ativa (moderada ou grave) da DII. A análise da curva ROC indicou que os pontos de corte de AF ≤5.042 para mulheres e ≤6.079 para homens podem ser usados para prever a redução da massa muscular. **Conclusão –** O AF pode ser considerado um preditor de redução de massa muscular nos pacientes com DII e ser utilizado para triagem e acompanhamento da evolução da desnutrição.

Palavras-chave – Ângulo de fase; desnutrição; doença inflamatória intestinal; massa muscular esquelética.

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