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### **ABOUT COVER**

Associate editor of World Journal of Hepatology, Dr. Yong-Ping Yang is a Distinguished Professor at Peking University Health Science Center in Beijing, China. Having received his Bachelor's degree from Yanbian University in 1985, Dr. Yang undertook his postgraduate training at PLA Medical College, receiving his Master's degree in 1992. He rose to Chief Physician in the Hepatology Division of the Fifth Medical Center of the Chinese PLA General Hospital in 2003 and has held the position since. His ongoing research interests involve liver fibrosis, cirrhosis and hepatocellular carcinoma, with a particular focus on cryoablation and cryo-immunotherapy for hepatocellular carcinoma. Currently, he serves as Chairman of the Department of Liver Disease of the Chinese PLA General Hospital and as President of the Chinese Research Hospital Association for the Study of the Liver Disease. (L-Editor: Filipodia)

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WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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**Retrospective Cohort Study** 

### ORIGINAL ARTICLE

# Phase angle and non-alcoholic fatty liver disease before and after bariatric surgery

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### Abstract

### BACKGROUND

Obesity is a global health problem that is continuing to increase in the young population. In Brazil, the frequency of obesity in 2018 was 19.8%. Several comorbidities are directly associated with obesity, such as non-alcoholic fatty liver disease (NAFLD), which is considered the most common liver disorder in Western countries and affects up to 46% of adults. Bariatric surgery is effective in treating obesity and can improve NAFLD; however, the effect of bariatric surgery on body composition, phase angle (PA), and improving NAFLD needs to be further studied.

### AIM

To analyze the PA in the postoperative period of bariatric surgery and to correlate it with changes in body composition and liver disease.



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### **METHODS**

This study is a retrospective cohort study of the analysis of the medical records of patients undergoing bariatric surgery in a reference center of a teaching hospital in Porto Alegre over a 2-year period. Patients older than 18 years whose record contained all information relevant to the study were included. The data analyzed were body composition and PA through electrical bioimpedance and NAFLD through liver biopsy in the pre- and postoperative period. The level of significance adopted for the statistical analyses was 5%.

### RESULTS

We evaluated 379 patients with preoperative data. Regarding PA, 169 patients were analyzed, and 33 patients had liver biopsy pre- and postoperatively with NAFLD information. In total, 79.4% were female, with a mean age of  $39.1 \pm 10.6$ years. The average body mass index (BMI) was  $45.9 \pm 7.5$  kg/m<sup>2</sup>. The PA showed a mean of  $5.8 \pm 0.62^{\circ}$  in the preoperative period and a significant reduction in the postoperative period. A postoperative reduction in body composition data (skeletal muscle mass, fat percentage, fat mass, body cell mass, BMI and visceral fat area) was shown as well. Regarding liver disease, all patients presented a reduction in the degrees and stages of liver disease in the postoperative period, and some had no degree of liver disease at all.

### **CONCLUSION**

PA decreased after bariatric surgery, with a direct correlation with weight loss and changes in body composition. The decrease in PA was not correlated with the improvement in NAFLD.

Key Words: Obesity; Body composition; Bariatric surgery; Phase angle; Non-alcoholic fatty liver disease; Liver disease

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**Core Tip:** We retrospectively evaluated 379 patients who underwent bariatric surgery, with non-alcoholic fatty liver disease in the preoperative period; we compared body composition, phase angle (PA) behavior and change in non-alcoholic fatty liver disease (NAFLD) in the pre- and postoperative period. There was an important improvement in body composition/body fat percentage and an improvement in NAFLD after bariatric surgery. Worsening PA was directly correlated with weight loss and skeletal muscle mass.

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## INTRODUCTION

Obesity is a complex chronic inflammatory disease characterized by excessive accumulation of body fat. It has multiple etiologies, such as biochemical, genetic, behavioral, social, environmental, and nutritional factors and imbalance between food intake and energy expenditure<sup>[14]</sup>. This disease presents its own pathophysiology as well as associated comorbidities<sup>[3,5]</sup>.

According to VIGITEL Brazil 2018<sup>[6]</sup>, the frequency of obese adults was 19.8% in a society that is aging and more ill. Obesity is closely associated with cardiovascular diseases, dyslipidemia, fatty liver, diabetes mellitus (DM) and other endocrine and metabolic disorders<sup>[1]</sup>. In obese people, a common comorbidity is non-alcoholic fatty liver disease (NAFLD).

NAFLD is defined as accumulation of fat in more than 5% of hepatocytes<sup>[7]</sup> without secondary cause, such as alcohol consumption (> 20 g for women and > 30 g for men,



daily), use of steatogenic medications, or hereditary disorders<sup>[8]</sup>.

The gold standard for the diagnosis of NAFLD is liver biopsy<sup>[9]</sup>, and its classification encompasses a wide spectrum of histopathological changes, from simple hepatic steatosis, which can evolve from non-alcoholic steatohepatitis (NASH), to cirrhosis and/or hepatocellular carcinoma<sup>[10]</sup>. Therefore, NAFLD, due to its different staging, may or may not present fibrosis in hepatocytes<sup>[11,12]</sup>. NAFLD is considered the most common liver disease in Western countries, affecting 90% of morbidly obese patients eligible for bariatric surgery<sup>[11]</sup>.

Because of the difficulty found in the clinical treatment of obesity, bariatric surgery is more efficient as a treatment option for individuals with severe obesity, when compared to non-surgical interventions<sup>[13]</sup>. Furthermore, surgical treatment shows improvement or remission in NAFLD<sup>[14]</sup>.

According to the Brazilian Society of Bariatric and Metabolic Surgery<sup>[15]</sup>, bariatric surgery combines techniques aimed to treat morbid obesity, severe obesity, and diseases associated with excess body fat or exacerbated by it. Gastric bypass surgery in Y by Roux (BPGYR) or Fobi-Capella surgery is the most commonly performed technique in Brazil and worldwide.

Electrical bioimpedance (BIA) is a method for analyzing body composition and is based on the principle of resistance and reactance that cells impose on the electrical current emitted by the device<sup>[16]</sup>. The human body is constituted of conductors like water and non-conductors, like body fat<sup>[17,18]</sup>.

Several parameters are measured using BIA, including body water, lean mass, fat mass, and phase angle (PA). BIA assesses nutritional status and can be a good method for prognostic evaluation, as it is practical, fast, non-invasive, and low cost<sup>[19]</sup>. However, body composition values in patients with dysmorphia (edema, ascites, and morbid obesity), as measured by BIA, may suffer interference. This is why PA has been widely used, since it is not associated with interference<sup>[20,21]</sup>.

Currently, there are segmented, multifrequency BIA devices with greater precision for assessing body composition in morbidly obese patients, as validated by Faria et al<sup>[22]</sup>.

PA was originally described by Baumgartner et al<sup>[23]</sup> for the diagnosis of metabolic disorders. It is a parameter applicable in clinical practice because it reliably helps to describe cell vitality and integrality. High values (up to 8°) may indicate body homeostasis, whereas values below 6°, depending on the disease, reflect a poor clinical prognosis, indicating changes in the selective permeability of the cell membrane<sup>[23,24]</sup>.

As already mentioned, PA reflects cellular integrity and functionality by measuring, through an electrical current, the values of resistance and reactance of the membrane of these cells, with skeletal muscle being a conductor of electrical current and the opposite occurring with fat mass<sup>[23-25]</sup>. In view of this fact, we believe that the body change resulting from bariatric surgery will reflect an improvement in NAFLD and can be measured by PA.

To date, there are not enough studies evaluating morbid obesity, body composition (described by the BIA), and associated comorbidities, such as NAFLD.

The present study aims to analyze the behavior of PA in the postoperative period of bariatric surgery, correlating it with changes in body composition and improvement of liver disease.

### MATERIALS AND METHODS

This is a retrospective cohort study that analyzed the medical records of patients undergoing bariatric surgery in a referral center of a teaching hospital in Porto Alegre. Patients over 18-years-old whose record contained all the information relevant to the study in the electronic or physical medical record were included. Patients who did not contain complete data were excluded. For convenience, the sample was carried out from July 2015 to July 2017. The data obtained were related to the protocol for routine pre- and postoperative care at the service's outpatient clinic.

### Electrical bioimpedance-PA and body composition

Data on body composition and weight were measured using BIA in all patients in the week preceding bariatric surgery without prior preparation. For BIA, the patient stood upright on the InBody 770 device from Ottoboni, with an electric current intensity of 80  $\mu$ A and 50/60 kHz frequency. The PA was obtained through the values of resistance and reactance through the formula: PA = tangent arc  $(Xc/R) \times 180/3.1416$ , described in the result sheet. The BIA was performed in a second step, and for



comparative postoperative analysis, we analyzed those patients who used the same BIA device 6 mo to 12 mo after bariatric surgery for routine postoperative evaluation.

### Anthropometric data-height and body mass index

Height was measured using a wall Tonelli stadiometer, model E150 A, with the patient standing upright and barefoot, with their feet together, and with their backs positioned against the wall. Body mass index (BMI) was calculated using the equation weight in kilograms, divided by height in meters squared and classified according to the World Health Organization<sup>[4]</sup>: BMI  $\ge$  30 kg/m<sup>2</sup> to 34.9 kg/m<sup>2</sup> Obesity Grade I, BMI between 35 kg/m<sup>2</sup> to 39.9 kg/m<sup>2</sup> Obesity Grade II, and BMI  $\ge$  40 kg/m<sup>2</sup> Obesity Grade III. The group of patients with a BMI greater than  $50 \text{ kg/m}^2$  was analyzed separately.

### Bariatric surgery

The bariatric surgery used was the BPGYR with intestinal derivation after monitoring and preparation with a multidisciplinary service team. All patients met the criteria for bariatric surgery. The surgeries were performed by four specialist surgeons, from the same team, trained and with much experience.

### Liver biopsy-NAFLD

Liver biopsies were routinely performed during the bariatric surgery trans operation by the surgeon under direct vision using a Tru-Cut needle at the beginning of the surgical procedure before liver withdrawal. The biopsies were analyzed by the same pathologist at the Hospital's Pathology Laboratory. The classification was made using the criteria of Kleiner et al<sup>[26]</sup>, as follows: Absence or presence of NAFLD and/or cirrhosis; steatosis activity (absent, discreet, moderate, accented, and massiveaccording to grade and location of the injury); ballooning and lobular inflammation; degrees of NASH (1, 2, 3, and 4), and fibrosis stages (1, 2, 3 and 4). The liver biopsies performed in the postoperative period were obtained by the same surgical team in patients who underwent a second intervention (cholecystectomy or appendectomy) in the period from 6 to 12 mo after bariatric surgery and analyzed in the same way as those of the first biopsy.

### Statistical analysis

Quantitative variables are described as mean and standard deviation or median and interquartile range. Categorical variables are described by absolute and relative frequencies.

To compare means before and after bariatric surgery, the t-student test for paired samples was applied. When comparing nominal categorical variables, the McNemar test was used and, for ordinals, the Wilcoxon test. To compare means between genders, the t-student test for independent samples was applied.

In the association between quantitative and ordinal variables, Pearson or Spearman correlation tests were used.

The level of significance adopted was 5% (P < 0.05), and the analyses were performed using the SPSS version 21.0 program (Armonk, NY, United States).

The project was elaborated in accordance with resolution 466 of 2012, which regulates the conduct of research in human beings, and submitted to and approved by the Research Ethics Committee under number 2.423.466. Patients who accepted to participate in the study signed the Informed Consent Term.

This study was reviewed by our specialist Biostatistics, Mestre, Ceres Andréia Vieira de Oliveira.

### RESULTS

Of the 727 patients operated on in the period, 379 who had complete preoperative information were allocated. For the analysis of data related to PA, 169 of these patients who underwent pre- and post-evaluation on the same device were allocated. Regarding NAFLD, we analyzed 33 patients who underwent postoperative liver biopsy.

Of the 379 patients, 79.4% were female, with a mean age of 39.1 ± 10.6 years and a BMI of  $45.9 \pm 7.5 \text{ kg/m}^2$ , classified as Obesity Grade III<sup>[4]</sup>. It is noteworthy that more than 22% of patients had a BMI greater than 50 kg/m<sup>2</sup>. Full-body PA showed an average of 5.89° ± 0.62°, with a minimum of 4.3° and a maximum of 7.9°. The other characteristics of the sample are shown in Table 1.



Table 1 Sample characteristics, <i>n</i> = 379	
Variables	n = 379
Gender, n (%)	
Male	78 (20.6)
Female	301 (79.4)
Age in yr, mean ± SD	39.1 ± 10.6
Weight in kg, mean ± SD	123.7 ± 24.8
Minimum	77
Maximum	235
BMI in kg/m <sup>2</sup> , mean $\pm$ SD	45.9 ± 7.5
BMI classification, <i>n</i> (%)	
30-34.99 kg/m <sup>2</sup>	3 (0.8)
35-39.99 kg/m <sup>2</sup>	82 (21.6)
40-49.99 kg/m <sup>2</sup>	210 (55.4)
50 kg/m <sup>2</sup> or more	84 (22.2)
SMM in kg, mean ± SD	34.1 ± 7.5
BCM in kg, mean ± SD	39.4 ± 8.3
Fat mass in kg, mean ± SD	62.6 ± 15.1
% Fat-mean ± SD	$50.7 \pm 4.6$
Visceral fat area in cm <sup>2</sup> , mean ± SD	243.7 ± 31.2
Phase angle °, mean ± SD	
Full-body	$5.89 \pm 0.62$
RA	5.58 ± 0.62
LA	$5.42 \pm 0.65$
Tr	7.97 ± 1.18
RL	$6.14 \pm 0.81$
LL	6.07 ± 0.84

BCM: Body cell mass; BMI: Body mass index; LA: Left arm; LL: Left leg; RA: Right arm; RL: Right leg; SD: Standard deviation; SMM: Skeletal muscle mass; Tr: Torso.

> All patients (n = 379) were diagnosed with NAFLD by liver biopsy, and the histological characteristics are shown in Table 2 Regarding the degrees of the disease, 78.1% had NASH and 43% fibrosis, ranging from F1 to F3. No patient had cirrhosis.

> The difference in pre- and postoperative body composition (n = 379) is found in Table 3, with all items statistically significant (P < 0.001).

> The associations of body composition variables with PA, stratified by gender (n =379), are shown in Table 4. In males, there was an inverse, statistically significant association between the percentage of fat, fat mass, and weight with PA in most body compartments, except the torso.

> In females, there was a negative, statistically significant association between the percentage of fat and PA in all compartments. There was a positive, statistically significant association between skeletal muscle mass (SMM) and body cell mass (BCM) with PA in most body compartments, except the legs.

> There was a negative, statistically significant association (r = -0.483; P < 0.001) between the reduction of full-body PA and the percentage of weight loss, as shown in Figure 1. There was a statistically significant positive association between the reduction of full-body PA with loss of SMM (r = 0.307; P < 0.001), as shown in Figure 2. The association of the reduction in PA of the whole body was also positive and significant with the loss of fat mass, (r = 0.280; P < 0.001), MCC (r = 0.287; P < 0.001), visceral fat area (r = 0.275; P < 0.001), BMI (r = 0.413; P < 0.001), and variation in the fat



Table 2 Sample characteristics for liver disease, <i>n</i> = 379	
Variables	n (%)
NAFLD	
Yes	379 (100.0)
No	0 (0.0)
Hepatic steatosis	
Absent	0 (0.0)
Discreet	159 (42.0)
Moderate	104 (27.4)
Accented	84 (22.2)
Massive	32 (8.4)
Ballooning	
Absent	91 (24.0)
Discreet	221 (58.3)
Moderate	18 (4.7)
Accented	49 12.9)
Massive	0 (0.0)
Lobular inflammation	
Absent	243 (64.1)
Discreet	100 (26.4)
Moderate	28 (7.4)
Accented	8 (2.1)
Massive	0 (0.0)
NASH	
Absent	83 (21.9)
Grade 1	201 (53.0)
Grade 2	67 (17.7)
Grade 3	28 (7.4)
Grade 4	0 (0.0)
Absent	216 (57.0)
Grade 1	86 (22.7)
Grade 2	44 (11.6)
Grade 3	33 (8.7)
Grade 4	0 (0.0)
Cirrhosis	
Yes	0 (0.0)
No	379 (100.0)

NAFLD: Non-alcoholic fatty liver disease; NASH: Non-alcoholic steatohepatitis.

percentage (*r* = 0.304; *P* < 0.001), as shown in Figure 3.

Men showed a more marked and significant reduction in the percentage of fat (-16 ± 4.9 vs -12.3 ± 5.3; P < 0.001) and visceral fat area (-110.7 ± 58.9 vs -90 ± 42.8; P = 0.024) when compared to women.

After bariatric surgery, a significant reduction in PA values (n = 169) was observed in all body compartments (P < 0.001), as described in Table 5.



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Verieklas	Pre	Post	P value	
Variables	mean ± SD	mean ± SD		
BMI in kg/m <sup>2</sup>	45.9 ± 7.5	$31.2 \pm 5.0$	< 0.001	
SMM in kg	34.1 ± 7.5	$29.0 \pm 6.4$	< 0.001	
BCM in kg	39.4 ± 8.3	33.9 ± 6.9	< 0.001	
Fat mass in kg	62.6 ± 15.1	31.9 ± 11.1	< 0.001	
% Fat	$50.7 \pm 4.6$	37.2 ± 8.1	< 0.001	
Visceral fat area in cm <sup>2</sup>	243.7 ± 31.2	$152.0 \pm 51.0$	< 0.001	

BCM: Body cell mass; BMI: Body mass index; SD: Standard deviation; SMM: Skeletal muscle mass.

Table 4 Association of body composition variables with phase angle in men and women, using Pearson's correlation coefficient, n = 379

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Variables	Weight in kg	SMM in kg	BCM in kg	Fat mass in kg	% Fat	Visceral fat area in cm <sup>2</sup>
Male gender, $n = 78$						
PA full body	-0.418 <sup>c</sup>	-0.118	-0.101	-0.469 <sup>c</sup>	-0.401 <sup>c</sup>	-0.075
PA RA	-0.299 <sup>b</sup>	-0.083	-0.064	-0.337 <sup>b</sup>	-0.287 <sup>a</sup>	-0.095
PA LA	-0.286 <sup>a</sup>	-0.031	-0.008	-0.349 <sup>b</sup>	-0.341 <sup>b</sup>	-0.136
PA Tr	-0.074	0.074	0.094	-0.134	-0.185	0.311 <sup>b</sup>
PA RL	-0.493 <sup>c</sup>	-0.179	-0.170	-0.531 <sup>c</sup>	-0.421 <sup>c</sup>	-0.101
PA LL	-0.509 <sup>c</sup>	-0.211	-0.209	-0.534 <sup>c</sup>	-0.403 <sup>c</sup>	-0.066
Female gender, $n = 301$						
PA full body	-0.106	0.125 <sup>a</sup>	0.122 <sup>b</sup>	-0.152 <sup>b</sup>	-0.393 <sup>c</sup>	-0.098
PA RA	0.011	0.169 <sup>b</sup>	0.148 <sup>a</sup>	-0.036	-0.245 <sup>c</sup>	-0.111
PA LA	0.043	0.193 <sup>b</sup>	0.155 <sup>b</sup>	-0.009	-0.226 <sup>c</sup>	-0.135 <sup>a</sup>
PA Tr	0.024	0.120 <sup>a</sup>	0.133 <sup>a</sup>	-0.030	-0.172 <sup>b</sup>	-0.058
PA RL	-0.154 <sup>b</sup>	0.083	0.068	-0.182 <sup>b</sup>	-0.406 <sup>c</sup>	-0.043
PA LL	-0.151 <sup>b</sup>	0.069	0.052	-0.187 <sup>b</sup>	-0.388 <sup>c</sup>	-0.086

 $^{a}P < 0.05$ 

 $^{b}P < 0.01.$ 

<sup>c</sup>P < 0.001. BCM: Body cell mass; LA: Left arm; LL: Left leg; PA: Phase angle; RA: Right arm; RL: Right leg; SMM: Skeletal muscle mass; Tr: Torso.

There was a statistically significant inverse association between BMI and full-body PA (P < 0.018), right leg and left leg (P < 0.001), as shown in Table 6. Regarding PA and NAFLD, there was no significant association (P > 0.05).

The analysis of the postoperative liver biopsy, compared with the preoperative biopsy of these patients (n = 33), showed that all of them had a reduction in the degrees and stages of liver disease, and 18.2% had no degree of liver disease (P < 0.05).

The other histological changes, which decreased from 75 to 90%, are described in Table 7. The body composition of this group (n = 33) showed that all parameters significantly decreased (P < 0.001) and that there was a reduction in PA in all compartments (P < 0.001), as described in Table 8.

There was a positive, statistically significant association between BMI  $(kg/m^2)$  and lobular inflammation (P < 0.05), NASH (P < 0.01), and fibrosis (P < 0.05). The other body composition variables did not correlate with the different histological characteristics of NAFLD.

There was an association between the variations of PA before and after bariatric surgery regarding the degree of lobular inflammation ( $r_s = -0.593$ ; P = < 0.001) but not



Table 5 Variation of phase angle in the pre- and postoperative period of bariatric surgery, <i>n</i> = 169				
Variables	Pre	Post	Puelue	— P value
	mean ± SD	mean ± SD	P value	
PA full body	$5.92 \pm 0.55$	$4.98\pm0.55$	< 0.001	
PA RA	$5.58\pm0.60$	$4.73 \pm 0.59$	< 0.001	
PA LA	$5.42 \pm 0.63$	$4.54\pm0.57$	< 0.001	
PA Tr	$7.87 \pm 1.15$	$6.76 \pm 1.29$	< 0.001	
PA RL	$6.25\pm0.66$	$5.19 \pm 0.65$	< 0.001	
PA LL	$6.18\pm0.70$	$5.14 \pm 0.66$	< 0.001	

LA: Left arm; LL: Left leg; PA: Phase angle; RA: Right arm; RL: Right leg; SD: Standard deviation; Tr: Torso.

### Table 6 Association of body mass index with phase angle through Pearson correlation, n = 169

Variables	ВМІ		
Variables	r	<i>P</i> value	
PA full body	-0.121	0.018	
PA RA	0.031	0.551	
PA LA	0.057	0.265	
PA Tr	0.054	0.298	
PA RL	-0.262	< 0.001	
PA LL	-0.262	< 0.001	

BMI: Body mass index; LA: Left arm; LL: Left leg; PA: Phase angle; r: Pearson's correlation coefficient; RA: Right arm; RL: Right leg; Tr: Torso.

steatosis ( $r_s = 0.305$ ; P = 0.095), ballooning ( $r_s = 0.057$ ; P = 0.760), NASH ( $r_s = -0.197$ ; P =0.288), and fibrosis ( $r_s = -0.183$ ; P = 0.324).

### DISCUSSION

Obese patients, candidates for bariatric surgery diagnosed with NAFLD, have been extensively studied<sup>[8,27-31]</sup>; and, to date, changes in lifestyle are the only effective forms of treatment for NAFLD. It was established that a loss of 7%-10% of body weight is necessary to present any change<sup>[32]</sup>. However, in order to guarantee body homeostasis, it is essential that the weight loss of these patients is the highest possible percentage of fat mass and not of SMM, preserving muscle volume and functionality. Therefore, BIA and PA are essential tools for monitoring the body characteristics and health of these patients<sup>[19,33]</sup>.

Most of our patients were women, with a mean age of 39.1 ± 10.6 years and a BMI of  $45.9 \pm 7.5 \text{ kg/m}^2$ , findings similar to those of Losekann *et al*<sup>[9]</sup>, who in 2013 analyzed 250 patients with liver biopsies performed in the bariatric surgery trans operation, which 80% were women, with a mean age of  $36.8 \pm 10.2$  years and a BMI of  $43.6 \pm 5.2$  $kg/m^2$ .

BMI is an analytical, non-laboratory method that is easy to apply and reproducible, allowing an indirect assessment of body composition, and is a defining parameter of indication for bariatric surgery.

The mean BMI after surgery decreased to  $31.2 \pm 5.0 \text{ kg/m}^2$  (P < 0.001), changing from Grade III Obesity to Grade I. The reduction in BMI was significant in both sexes, with no significant difference between them. All body composition parameters had a significant decrease (P < 0.001), mainly on fat mass and visceral fat area. In the present study, men compared to women showed a more marked and significant reduction in the percentage of fat and in the area of visceral fat.

Perrone *et al*<sup>[34]</sup> reported that the decrease in BMI after bariatric surgery in men was



Table 7 Degrees and staging of r			.,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Variables	Pre	Post	
	n (%)	n (%)	
NAFLD			0.031
Yes	33 (100)	27 (81.8)	
No	0 (0.0)	6 (18.2)	
Hepatic steatosis			< 0.001
Absent	0 (0.0)	6 (18.2)	
Discreet	14 (42.4)	24 (72.7)	
Moderate	8 (24.2)	3 (9.1)	
Accented	8 (24.2)	0 (0.0)	
Massive	3 (9.1)	0 (0.0)	
Ballooning			< 0.001
Absent	5 (15.2)	29 (87.9)	
Discreet	23 (69.7)	4 (12.1)	
Moderate	3 (9.1)	0 (0.0)	
Accented	2 (6.1)	0 (0.0)	
Lobular inflammation			0.003
Absent	21 (63.6)	30 (90.9)	
Discreet	7 (21.2)	3 (9.1)	
Moderate	3 (9.1)	0 (0.0)	
Accented	2 (6.1)	0 (0.0)	
NASH			< 0.001
Absent	6 (18.2)	25 (75.8)	
Grade 1	20 (60.6)	5 (15.2)	
Grade 2	4 (12.1)	3 (9.1)	
Grade 3	3 (9.1)	0 (0.0)	
Fibrosis			0.033
Absent	26 (78.8)	27 (81.8)	
Grade 1	3 (9.1)	4 (12.1)	
Grade 2	0 (0.0)	0 (0.0)	
Grade 3	4 (12.1)	2 (6.1)	

NAFLD: Non-alcoholic fatty liver disease; NASH: Non-alcoholic steatohepatitis.

greater than that in women, without influencing the improvement of comorbidities in the long term, because the BMI does not differentiate or qualify weight loss, which should be mostly fat and not SMM. A study by Hartwig *et al*<sup>[36]</sup>, showed similar results in men and women regarding the decrease in the percentage of fat and fat mass in the postoperative period. De Paris *et al*<sup>[36]</sup> showed a reduction in body composition (weight, fat-free mass, SMM, fat mass, and fat percentage) in the postoperative period of bariatric surgery, results similar to ours.

All of our patients had NAFLD; accentuated or massive steatosis in 30.6%; ballooning in 76%; lobular inflammation in 35.9%; NASH in 78.1%; fibrosis in 43%; and no case of cirrhosis. NAFLD patients are obese<sup>[37]</sup>, with a prevalence of 51% of cases<sup>[38]</sup>. In patients with obesity undergoing bariatric surgery, the percentage of steatosis ranged from 87.6% to 100%<sup>[8,27.31]</sup>, ballooning from 58.9% to 88%<sup>[29,30]</sup>, lobular inflammation from 23% to 88%<sup>[29,31]</sup>, and fibrosis from 31% to 44.9%<sup>[28,29,31]</sup>, findings

Table 8 Phase angle and body composition in patients who underwent liver biopsy after bariatric surgery, <i>n</i> = 33				
Variables	Pre	Post	Duralua	
Variables	mean ± SD	mean ± SD	<i>P</i> value	
BMI in kg/m <sup>2</sup>	$45.2 \pm 6.9$	$31.8 \pm 5.4$	< 0.001	
SMM in kg	$31.9 \pm 6.8$	$27.1 \pm 5.3$	< 0.001	
BCM in kg	$37.0 \pm 7.8$	32.1 ± 5.9	< 0.001	
Fat mass in kg	$60.7 \pm 13.3$	33.6 ± 11.1	< 0.001	
% Fat	$51.6 \pm 3.5$	39.8 ± 8.2	< 0.001	
Visceral fat area in cm <sup>2</sup>	$249.3 \pm 23.1$	$162.5 \pm 52.3$	< 0.001	
PA full body °	$5.93 \pm 0.65$	$4.91\pm0.60$	< 0.001	
PA RA °	$5.55 \pm 0.77$	$4.61\pm0.64$	< 0.001	
PA LA °	$5.44 \pm 0.86$	$4.44\pm0.58$	< 0.001	
PA Tr °	$7.84 \pm 1.24$	$6.73 \pm 1.03$	< 0.001	
PA RL °	$6.42\pm0.72$	$5.18 \pm 0.68$	< 0.001	
PA LL °	$6.38\pm0.74$	$5.19 \pm 0.66$	< 0.001	

BCM: Body cell mass; BMI: Body mass index; LA: Left arm; LL: Left leg; PA: Phase angle; RA: Right arm; RL: Right leg; SMM: Skeletal muscle mass; Tr: Torso.

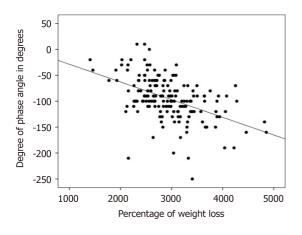


Figure 1 Association between the percentage of weight loss with the reduction of the phase angle in the postoperative period of bariatric surgery (n = 169).

similar to ours.

Some NAFLD patients present progression from simple steatosis to advanced stages, such as NASH and fibrosis, increasing the risk of cirrhosis and hepatocellular carcinoma. In addition, it is believed that NAFLD is implicated in the pathogenesis of type 2 DM and cardiovascular diseases<sup>[32]</sup>. These facts are fundamental in the search for the reduction of obesity that bariatric surgery provides.

We found a direct association between BMI and lobular inflammation, NASH, and fibrosis (P < 0.05), which is why it is important to monitor evolution of this group of patients.

The assessment of body composition is limited in several clinical conditions; and, therefore, the use of BIA data has gained increasing attention<sup>[39]</sup>. PA can be used as a biomarker for lean mass and/or for reducing muscle mass<sup>[39-41]</sup>, besides being recognized as a marker of malnutrition<sup>[40,41]</sup> and predictor of morbidity and mortality in several diseases<sup>[18,42]</sup>.

The PA of healthy individuals can vary between 6° and 7°, according to Bosy-Westphal et al<sup>[43]</sup> and 6.96° according to Barbosa-Silva et al<sup>[44]</sup>. There is no reference value that classifies PA for patients with obesity who have NAFLD. In the studied population, the PA was  $5.89 \pm 0.62^\circ$ , lower than the values described above, probably



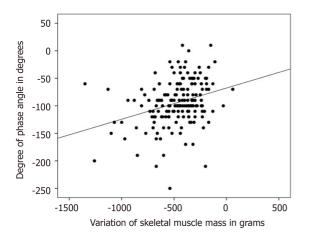


Figure 2 Association between the variation in skeletal muscle mass with the reduction of phase angle in the postoperative period of bariatric surgery (n = 169).

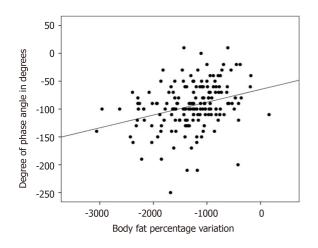


Figure 3 Association between the reduction in the percentage of body fat with the reduction in phase angle in the postoperative period of bariatric surgery (*n* = 169).

due to obesity.

In Table 4, we evaluated the associations of PA with the variables of body composition, and we observed in men a significant negative relation with decreased weight, fat mass, and percentage of fat (P < 0.01). In women, this relation of PA was with the decrease in the percentage of fat (P < 0.01). There was a significant positive relation with SMM and BCM (P < 0.05). PA decreased in most variables related to weight loss (P < 0.05). Baumgartner *et al*<sup>[45]</sup>, in 1988, observed a statistically significant negative correlation of PA with the percentage of body fat, corroborating the findings of our study. A study by Peres *et al*<sup>[46]</sup> analyzed 66 patients over 18 years of age with NAFLD, chronic hepatitis, cirrhosis, and hepatocellular carcinoma who had a mean PA of 5.1°, values similar to those found in the present study.

The post-surgical evaluation showed that PA decreased significantly in all evaluated segments (P < 0.001), as shown in Table 5, and its correlation with BMI showed a significant difference (P = 0.018), as shown in Table 6. These are apparently paradoxical findings, based on knowledge that the highest PA means improvement and the lowest means clinical worsening. We must consider the time of the second assessment, within the first year, as directly related to the decrease. A new evaluation of PA, at a longer time point, already programmed, may show an increase in PA.

Norman *et al*<sup>[47]</sup> described that BMI is one of the biological factors that influences PA. Furthermore, Llames *et al*<sup>[33]</sup> found a reduction in PA in individuals with a BMI greater than 35 kg/m<sup>2</sup>. Bosy-Westphal *et al*<sup>[43]</sup> showed that PA increased with an increase in BMI up to 30 kg/m<sup>2</sup> and that such physiological behavior can be explained as a reflection of the increase in the number of cells (adipocytes and myocytes), since the reactivity of BIA is dependent on the amount of cell membranes. The same study

showed that with BMI above  $40 \text{ kg/m}^2$ , there was an inverse relation between PA and BMI. The explanation is that severe obese individuals have a loss of functionality in the cell membrane, which may contribute to the decrease in PA.

In 2017, Vassilev et al<sup>[48]</sup> in Germany, with 173 patients undergoing bariatric surgery (BPGYR), showed a correlation between PA and weight loss, between 6 and 12 mo postoperatively, and a significant reduction in lean mass with a reduction in PA, results similar to ours. Koehler et al<sup>[49]</sup>, with 20 patients undergoing bariatric surgery (BPGYR), showed significant results in reducing PA, at an earlier time, from 3 to 6 mo.

In the present study, there was a negative association between the reduction of fullbody PA and the percentage of weight loss (P < 0.001), as shown in Figure 1. There was a positive association between the reduction of full-body PA with the variation of SMM (P < 0.001), as shown in Figure 2; and there was a positive association between the reduction of PA of the whole body and the percentage variation of fat (P < 0.001), as shown in Figure 3. These same associations were observed in the other parameters (loss of fat mass; BCM; visceral fat area, BMI), all with significant value (P < 0.001).

In the Vassilev et al study<sup>[48]</sup>, the higher the percentage of body fat in the postoperative period, the lower the PA, and the reduction in BCM occurred with a reduction in PA after 9 mo of surgery. Thus, it is clear that the percentage of fat, even after weight loss, continues to have a negative influence on PA. The decrease in PA in the postoperative period is linked to weight loss, which can be a confusing factor when relating the reduction in the percentage of fat and PA, since the present study also associated a reduction in BMI with a decrease in PA.

There was an association between the variations of PA before and after bariatric surgery regarding the degree of lobular inflammation ( $r_s = -0.593$ ; P = < 0.001) but not with steatosis ( $r_s = 0.305$ ; P = 0.095), ballooning ( $r_s = 0.057$ ; P = 0.760), NASH ( $r_s = -0.197$ ; P = 0.288), and fibrosis (r<sub>s</sub> = -0.183; P = 0.324).

Regarding the role of PA and NAFLD staging, Peres et al<sup>[46]</sup> found no difference in PA values in patients with different degrees and stages of liver disease; our findings did not show significance associating the decrease in PA with the variation in the degree of steatosis, ballooning, NASH, and fibrosis in the pre- and postoperative period, demonstrating that the improvement of liver disease after bariatric surgery is not related to the worsening of PA.

The comparison of liver histology before and after surgery (n = 33) showed a significant improvement in NAFLD, where 18.2% had no degree of liver disease (P =(0.031); all parameters analyzed showed a reduction in histological changes, from 75%to 90% (P < 0.05), as described in Table 7.

Máttar et al<sup>[24]</sup> analyzed patients undergoing different bariatric surgery techniques and observed significant improvement in steatosis (from 88% to 8%), lobular inflammation (from 23% to 2%), and fibrosis (31% to 13%). In addition, 37% no longer had lobular inflammation, and 20% had no fibrosis, in line with our study. Similar data were found in Cazzo et al<sup>[50]</sup> review in 2017 with patients undergoing bariatric surgery using different surgical techniques<sup>[27,30,51-53]</sup>.

A pioneering study by Silverman et al<sup>[54]</sup> in 1995 observed an improvement in liver disease in the postoperative period of bariatric surgery with the same surgical technique we used, with a 71% reduction in steatosis; 19% absence of steatosis; 76.9% absence of fibrosis, and 7.6% reduction in fibrosis, corroborating with our findings. There was a marked change in body composition in this group (n = 33), in all parameters (P < 0.001), as well as a reduction in PA (P < 0.001), as shown in Table 8. These data reinforce that weight loss is fundamental in the treatment of NAFLD.

### CONCLUSION

The PA decreased after bariatric surgery, with a direct correlation with weight loss and changes in body composition. Grade III obesity became Grade I obesity. The decrease in the PA after bariatric surgery did not correlate with the improvement of NAFLD, even with the marked improvement of NAFLD. The decrease in the PA after performing bariatric surgery correlated with the decrease in the BMI, loss of SMM, and decreases in body fat (in percentages and kilograms), BCM, and visceral fat area.

We believe that PA should increase with more time after bariatric surgery, since the change in the body composition of the operated patient will reflect an improvement in body mass distribution and, consequently, less inflammatory process. An important point is what form of protein supplementation should be used with these patients after surgery in order to minimize the loss of muscle mass and thereby increase PA. With the data presented in this study, we suggest that PA may be a marker of the state of

### body composition linked to the functionality of SMM.

### ARTICLE HIGHLIGHTS

### Research background

Obesity is a complex chronic inflammatory disease characterized by excessive accumulation of body fat. In obese people, a common comorbidity is non-alcoholic fatty liver disease (NAFLD). NAFLD is considered the most common liver disease in Western countries, affecting 90% of morbidly obese patients eligible for bariatric surgery. To evaluate this patients, bioimpedance (BIA) can be a good method for nutritional and prognostic evaluation, using phase angle (PA).

### Research motivation

There are not enough studies to evaluate morbid obesity, its body composition (described by the BIA), and associated comorbidities, such as NAFLD. We believe that the body change resulting from bariatric surgery will reflect an improvement in NAFLD and can be measured by PA, since it reflects cellular integrity and functionality by measuring, through an electrical current, the values of resistance and reactance of the membrane of these cells, with skeletal muscle being a conductor of electrical current and the opposite occurring with fat mass.

### Research objectives

The aim of this study was to analyze the behavior of PA in the postoperative period of bariatric surgery, correlating it with changes in body composition and improvement of liver disease.

### Research methods

This was a retrospective cohort study that analyzed the medical records of 727 patients undergoing bariatric surgery in a referral center of a teaching hospital in the south of Brazil. For convenience, the sample was carried out from July 2015 to July 2017. The data obtained were related to the protocol for routine pre- and postoperative care at the service's outpatient clinic. Quantitative and categorical variables analyses were performed to assess the association between PA, NAFLD, and body composition before and after bariatric surgery.

### Research results

We analyzed 727 patients' medical records, and 379 patients were selected for having all preoperative data. Regarding PA, 169 patients were analyzed, and 33 patients had liver biopsy pre-and postoperatively with NAFLD information. The PA showed a significant reduction in the postoperative period as well as body composition data. Regarding liver disease, all patients presented a reduction in the degrees and stages of liver disease in the postoperative period, and some had no degree of liver disease.

### Research conclusions

The PA decreased after bariatric surgery, with a direct correlation with weight loss and changes in body composition, and it did not correlate with the improvement of NAFLD. With the data presented in this study, we suggest that PA may be a marker of the state of body composition linked to the functionality of skeletal muscle mass.

### Research perspectives

Performing large scale prospective studies with long-term follow-up are needed to verify if PA increases with more time after bariatric surgery, since the change in the body composition of the operated patient will reflect an improvement in body mass distribution and, consequently, less inflammatory process.

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