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ORIGINAL ARTICLE

Heart Failure: Correlation between Anthropometric Parameters, Body Composition and Cell Integrity

Tathiana Carestiato Faria, Denise Tavares Giannini, Patrícia Vasconcelos Fontana Gasparini, Ricardo Mourilhe Rocha

Hospital Universitário Pedro Ernesto da Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ – Brazil

Abstract

Background: Knowledge about phase angle and its use as a prognostic determinant in patients with heart failure is still scarce.

Objective: To evaluate the correlation between anthropometric indicators, cardiac function and cell integrity in patients with heart failure with reduced ejection fraction.

Methods: This was a cross-sectional study that evaluated patients with heart failure with reduced ejection fraction by anthropometry and bioelectrical impedance analysis. Chi-square test and Student's t test were used to analyze differences, and Pearson's linear correlation was used to evaluate associations, using $p < 0.05$ to indicate statistical significance.

Results: We evaluated 41 subjects aged 30-74 years, of which 34 were men (82.9%). Mean phase angle was higher among women (7.1%), but significant differences between men and women were found only for body fat percentage. Phase angle correlated with body mass index ($r = 0.44$, $p = 0.004$) and there was a trend of correlation of the phase angle with waist-to-height ratio ($r = 0.29$, $p = 0.06$) and the left ventricular ejection fraction ($r = 0.29$, $p = 0.07$).

Conclusions: Phase angle showed a good correlation with body mass index and showed a trend of correlation with the left ventricular ejection fraction, supporting the obesity paradox and the prognostic importance of this marker. Further studies on the applicability of the phase angle in the prognosis of these patients are still needed. (International Journal of Cardiovascular Sciences. 2018;31(3)226-234)

Keywords: Heart Failure; Body Composition; Obesity; Stroke Volume; Body Mass Index.

Introduction

Systemic arterial hypertension (SAH) and coronary artery disease (CAD) are common causes of heart failure (HF). One of their main risk factors is obesity, which causes several adverse effects to health, particularly to cardiovascular health.[1]

According to the International Diabetes Federation (IDF),[2] although increased body mass index (BMI) may lead to these conditions, excessive abdominal fat, estimated by waist circumference (WC), is the main indicative of metabolic syndrome. Therefore, central body fat has been increasingly recognized as an independent risk for cardiovascular disease (CVD).[3]

On the other hand, in established HF, mild to moderate overweight has been associated with a substantial increase in survival as compared with normal weight individuals, the so called "obesity paradox".[1,4] One of the several theories that may explain such paradox is the fact that excessive adipose tissue provides greater storages that may exert a protect role against disease-related metabolic changes that may lead to cardiac cachexia. Cardiac cachexia is a syndrome that involves progressive weight loss and changes in body composition, bearing a devastating prognosis for HF patients.[4]

Besides, most data related to this paradox identify obesity by BMI,[4] which although is the most widely used method in nutritional assessment, does not clearly reflect

Mailing address: Denise Tavares Giannini
Rua Gustavo Corção, 606 apto: 301. Postal Code: 22790-150, Recreio dos Bandeirantes, Rio de Janeiro, RJ – Brazil.
E-mail: denisegiannini@uol.com.br

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individual's body composition, and has a relatively low sensitivity in predicting excessive body fat.[5] In this context, other nutritional assessment methods may be used, such as densitometry by dual-energy X-ray absorptiometry (DXA) and computed tomography (CT). These methods, however, although more accurate, are also more costly and complex.[6]

When these recommended methods are not available, some anthropometric measures and indexes seem to be good alternatives for estimating body composition. In addition to WC, the conicity index (C-index), proposed by the World Health Organization (WHO) to evaluate obesity and body fat distribution is of equal importance.[7] Also, waist-to-height ratio (WHtR), which is based on the assumption that for each height, there is an acceptable level of fat stored in the upper body, has also a good relationship with central body fat.[8]

Bioelectrical impedance analysis (BIA) has also been widely used, especially due to the high data processing speed, its non-invasiveness, easiness of use and relatively low cost. BIA provides estimates of fat mass and fat-free mass components using predictive equations, and of phase angle (PA).[9,10]

Left ventricular ejection fraction (LVEF) is another parameter to be evaluated in these patients due to its prognostic importance. Its reduction is associated with lower survival, and distinction of HF patients with (HFREF) and without reduced ejection fraction is increasingly required because of different clinical manifestations and forms of treatment for each case.[11]

Therefore, due to the association between obesity and cardiovascular changes, assessment of HFREF by methods that estimate not only total fat, but also central fat, is extremely relevant. Besides, the applicability of PA in HF has not been well established in the literature.

Thus, the aim of the present study was to evaluate the relationship between anthropometric indicators, cardiac function and cell integrity in HFREF.

Methods

This was a cross-sectional study of patients treated at the Heart Failure Outpatient Center of Pedro Ernesto University Hospital.

A convenience sample was used, and HFREF of both sexes, aged from 18 to 74 years were considered eligible. Exclusion criteria were patients with clinical evidence of edema and ascites, amputee patients and patients using pacemakers. Patients with a BMI lower than 16 kg/m^2 or greater than 34 kg/m^2 were also excluded, because estimation of body composition by most of BIA predictive equations using these BMI values is not considered reliable.[12] We also excluded patients who did not meet the standardized BIA protocol, and those with a higher percentage of extracellular water compared with intracellular water, indicating a water imbalance that had not been identified at the physical exam,[9] and patients with an electrocardiography performed longer than one year before the date of the anthropometric assessment.

Outcome measures were: sex, age, LVEF (electrocardiography), etiology of the disease, functional class (New York Heart Association, NYHA),[13] comorbidities, previous myocardial revascularization surgery (MRS), valve replacement, stent implantation, acute myocardial infarction (AMI), and anthropometric parameters (body mass, kg; height, m; WC, cm; BMI, kg/m^2; WHtR and C index), measured by one trained examiner.

Body mass was measured using a digital medical scale (Welmy®) with maximum capacity of 200 kg at the nearest 0.1kg. Height was measured to the nearest 0.1 cm using a wall mounted stadiometer (Sanny®, 220 cm). Measurements were performed as proposed by Lohman et al.[14]

WC was measured using an inelastic tape at the nearest 0.1 mm, according to the IDF criteria.[15] Patients were divided into the following groups – WC $\geq$ 80 cm and < 80 cm for women; WC $\geq$ 90 cm and < 90 cm for men.

WHtR was calculated by dividing WC (cm) by height (cm), and the cutoff points adopted were 0.52 for men and 0.53 for women. C-index was obtained according to the equation proposed by Valdez,[16] with the cutoff points of 1.25 and 1.18 for men and women, respectively. The WHtR and the C-index cutoff points indicating an increased coronary risk were defined based on the study by Pitanga and Lessa.[17]

Nutritional diagnosis was determined by BMI, which was calculated by dividing body mass by height squared and classified according to the WHO criteria.[18]

Body composition and cell integrity were evaluated by tetrapolar BIA (Biodynamics 450®), according the Brazilian Medical Association criteria.[12] BIA results of PA and body fat percentage (BF%) were used for analyses. For BF% classification, we used the cutoff points of 25% for men and 32% for women.[19]

The study was approved by the Research Ethics Committee of the institution (approval number 47828915.3.0000.5259). All patients were informed about the study's purpose, and signed an informed consent form before being included, as volunteers, in the study.

Statistical analysis

Normality of the variables was tested by the Kolmogorov-Smirnov test. Descriptive statistics was used for characterization of the sample. Continuous variables were expressed as mean and standard deviation (±SD); the Student's t-test and the Pearson correlation were used to analyze differences and correlations between independent samples, respectively. Categorical variables were expressed as percentage, and associations between them were analyzed by the chi-square test or the Fisher's exact test. Analyzes were performed using the STATA 14 softwae, and statistical significance was set at $p < 0.05$.

Results

In the present study, 41 volunteers of both sexes (n = 34, 82.9% were men) aged 61 ± 10.8 years were studied.

The most common comorbidity was SAH (n = 33; 80.5%), followed by DM (n = 21, 51.2%), chronic kidney disease (n = 3; 7.3%) and chronic obstructive pulmonary disease (n = 3, 7.3%).

With respect to HF classification, NYHA functional class I was the most prevalent (n = 18, 43.9%), and 34.1% (n = 14) of patients had ischemic HF. Eighteen (43.9%) patients had previous AMI, 14.6% (n = 6) had previous MRS, 9.8% (n = 4) had previous valve replacement, and 21.9 (n = 9) had previous stent implantation. No differences were found between men and women, except for the prevalence of DM, which was higher in women (n = 6, 85.7%) than men (n = 15, 44.1%) (Table 1).

Regarding the anthropometric variables, BF% was significantly lower in men (mean of 27.2%) than women (mean of 35.8%). No differences were found in the other anthropometric parameters between men and women. PA (7.1° ± 1.4), estimated by BIA, and LVEF (37.4%) were higher in women than men, with no significant difference though. Clinical and anthropometric characteristics of the study population are described in Table 2.

Mean BMI was 26.4 ± 3.6 Kg/m², with no difference between men (26.4 ± 3.4 Kg/m²) and women (26.5 ± 4.8 Kg/m²) (Table 2). Most participants were overweight (41.5%), followed by normal weight (39.0%) and obese subjects (19.5%).

Anthropometric indicators of obesity (Table 3) showed that 61.8% of men and 57.1% of women were overweight/obese, and 100% of women and 91.2% of men were at increased risk according to the C-index (totaling 92.7% of the study population). According to WC, 82.4% of men and 85.7% of women were at increased risk, and 76.5% of men had increased WHtR. With respect to BF%, 67.7% of men and 71.4% of women were obese. No statistically significant difference in any of the indicators was found between men and women.

Table 4 shows the correlation between obesity anthropometric indicators, PA and LVEF of the studied population. BMI showed a significant positive correlation with C-index, WC, WHtR, BF%, and PA; there was a positive significant correlation of C-index with WC, WHtR and BF%, a positive significant correlation of WC with BF% and WHtR, and between WHtR and BF%. The strongest correlations were observed of BMI with WC (r = 0.84) and WHtR (r = 0.83), of C index with WC (r = 0.80) and WHtR (r = 0.81), and between WC and WHtR (r = 0.85). PA showed a significant correlation with BMI and a marginal correlation with WHtR (r = 0.29, 0.06) and LVEF (r = 0.29, p = 0.07).

Discussion

Some studies have demonstrated the relationship of excess weight with left ventricular hypertrophy and concentric and eccentric remodeling, and with diastolic dysfunction followed by long-term systolic dysfunction,[20,21] indicating a direct effect of body composition on cardiovascular system.

In this context, anthropometric assessment is crucial in the clinical practice, since an early diagnosis of obesity and an adequate intervention contribute to improve patients' quality of life and prevent the worsening of health.[22] Borné et al.[23] investigated 26,653 individuals aged 45-73 years and showed that increased BMI, WC and BF% increased the risk of hospitalization for HF, and that this risk was even greater with combined exposure to both increased BMI and WC.

In our study, mean BMI was 26.4 ± 3.4 Kg/m², and most patients (41.5%) were overweight. Gastelurrutia et al.[24] evaluated HFREF and patients without reduced ejection fraction and identified that 42% of patients were overweight and 27% were obese. Although BMI has been used as an important indicator of body composition in epidemiologic studies, individual BMI values should be interpreted with caution.[10] Different from the general population, in HF patients, BMI is inversely correlated

Table 1 – Comorbidities, heart failure etiology, New York Heart Association (NYHA) functional class, previous acute myocardial infarction and previous surgeries by sex in the study population (n = 41)

	Men (n=34)	Women (n=7)	Total (n=41)	p-value*
	n (%)	n(%)	n(%)	
Comorbidities				
SAH	27 (79.4)	6 (85.7)	33 (80.5)	0.7
DM	15 (44.1)	6 (85.7)	21 (51.2)	0.04
CKD	2 (5.9)	1 (14.3)	3 (7.3)	0.4
COPD	3 (8.8)	0 (0.0)	3 (7.3)	0.4
HF etiology				
Ischemic	12 (35.3)	2 (28.6)	14 (34.1)	0.7
Non-ischemic	22 (64.7)	5 (71.4)	27 (65.9)	
FC (NYHA)				
I	16 (47.1)	2 (28.6)	18 (43.9)	
II	11 (32.3)	2 (28.6)	13 (31.7)	0.2
III	7 (20.6)	2 (28.6)	9 (22.0)	
IV	0 (0.0)	1 (14.2)	1 (2.4)	
AMI				
Yes	16 (47.1)	2 (28.6)	18 (43.9)	0.4
No	18 (52.9)	5 (71.4)	23 (56.1)	
Surgery				
MRS	6 (17.6)	0 (0.0)	6 (14.6)	0.2
VR	3 (8.8)	1 (14.3)	4 (9.8)	0.7
Stent implantation	8 (23.5)	1 (14.3)	9 (21.9)	0.6

**comparison between men and women. SAH: systemic arterial hypertension; DM: diabetes mellitus; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; HF: heart failure; FC: functional class; AMI: acute myocardial infarction; MRS: myocardial revascularization surgery; VR: valve replacement*

with mortality and rehospitalization.[25] However, some studies have shown that not only BMI but also other anthropometric variables should be used in the assessment of HF patients, for a better assessment of body compartments and central obesity.[24,26]

BIA has been currently validated to estimate body composition and nutritional status in healthy individuals, and in several clinical conditions, including malnutrition and chronic diseases.[9] The validity of its use in HF patients has been questioned, since the method is known to be influenced by the amounts of body fluids, and to not be appropriate for situations of altered hydration of tissues.[12,25] Therefore, in our study, we used standardization criteria for BIA; only stable patients participated in the study, and those with altered hydration were excluded.[12] According to BF% measured by this method, 67.7% of men and 71.4% of women were identified as obese, corresponding to the majority (68.3%) of the study population.

Central obesity indicators are positively correlated with the amount of visceral adipose tissue and cardiometabolic disorders.[25] Our subjects had excess central adiposity according to all indicators studies (WC, C-index and WHtR). Similar findings were

Table 2 – Clinical and anthropometric variables of the study population, by sex

Variables	Men (n = 34)	Women (n = 7)	Total (n = 41)	p-value *
	Mean (±SD)	Mean (±SD)	Mean (±SD)	
Age (years)	60.5 (11.3)	63 (8.7)	61 (10.8)	0.29
BMI (Kg/m²)	26.4 (3.4)	26.5 (4.8)	26.4 (3.6)	0.48
WC (cm)	96.8 (11.4)	93.6 (13.0)	96.3 (11.6)	0.26
WHtR	0.57 (0.06)	0.61 (0.1)	0.57 (0.07)	0.05
C-index	1.32 (0.09)	1.35 (0.08)	1.32 (0.09)	0.22
BF%	27.2 (4.3)	35.8 (4.6)	28.7 (5.4)	< 0.001
PA (°)	6.7 (1.0)	7.1 (1.4)	6.8 (1.1)	0.18
LVEF (%)	34.5 (8.6)	37.4 (7.3)	35.0 (8.4)	0.21

**comparison between men and women. SD: standard deviation; BMI: body mass index; C-index: conicity index; WC: waist circumference; WHtR: waist-to-height-ratio; BF%: body fat percentage; PA: phase angle; LVEF: left ventricular ejection fraction*

Table 3 – Obesity anthropometric indicators in the study population by sex

Variables	Men	Women	Total	p-value*
	n(%)	n(%)	n (%)	
BMI				
Normal weight	13 (38.2)	3 (42.9)	16 (39.0)	0.09
Overweight/obesity	21 (61.8)	4 (57.1)	25 (61.0)	
C-index				
Normal	3 (8.8)	0 (0.0)	3 (7.3)	0.4
Increased	31 (91.2)	7 (100.0)	38 (92.7)	
WC				
Normal	6 (17.6)	1 (14.3)	7 (17.1)	0.8
Increased	28 (82.4)	6 (85.7)	34 (82.9)	
WHtR				
Normal	8 (23.5)	2 (28.6)	10 (24.4)	0.8
Increased	26 (76.5)	5 (71.4)	31 (75.6)	
BF%				
Normal	11 (32.3)	2 (28.6)	13 (31.7)	0.8
Obesity	23 (67.7)	5 (71.4)	28 (68.3)	

**comparison between men and women. BMI: body mass index; C-index: conicity index; WC: waist circumference; WHtR: waist-to-height-ratio; BF%: body fat percentage.*

Table 4 – Correlation between obesity anthropometric indicators, phase angle and left ventricular ejection fraction

	BMI	C-index	WC	WHtR	BF%	PA
BMI						
C-index	(0.46)					
p-value	0.002					
WC	(0.84)	(0.80)				
p-value	< 0.001	< 0.001				
WHtR	(0.83)	(0.81)	(0.85)			
p-value	< 0.001	< 0.001	< 0.001			
BF%	(0.36)	(0.38)	(0.32)	(0.53)		
p-value	0.02	0.01	0.04	< 0.001		
PA	(0.44)	(-0.01)	(0.22)	(0.29)	(0.06)	
p-value	0.004	0.95	0.17	0.06	0.7	
LVEF	(0.17)	(0.12)	(0.15)	(0.17)	(0.23)	(0.29)
p-value	0.29	0.47	0.34	0.29	0.15	0.07

BMI: body mass index; C-index: conicity index; WC: waist circumference; WHtR: waist-to-height-ratio; BF%: body fat percentage; PA: phase angle; LVEF: left ventricular ejection fraction

reported in the study by Quirino et al.[27] showing that mean WC and WHtR values were higher than recommended in both men and women.

Regarding the analysis of associations between anthropometric variables, Gomes et al.[28] found a positive significant correlation between BMI and WC. Colombo et al.[29] showed that BMI had a positive significant correlation with BF%, obtained by the sum of skinfold thickness measures, and both BMI and BF% had a significant correlation with WC. These correlations were found in our study also.

Lobato et al.,[30] found correlations between BMI and WC, and positive significant correlations of WC with WHtR and C-index, and between WHtR and C-index. In the study by Mendes et al.,[31] involving patients with diabetes mellitus (DM), obesity and/or SAH, BMI was positively correlated with BF% ($p < 0.001$) and C-index ($p = 0.009$).

Studies on C-index and WHtR as coronary risk predictors have been carried out in the Brazilian population and demonstrated the importance of these indicators in diagnostic assessment of patients.[15,17]

We also obtained PA measures using BIA. These parameters have been increasingly used as a diagnostic tool in the clinical practice. In our study group, mean PA was 6.8º ± 1.1, with greater values in women (7.1º ± 1.4), but not significantly different than men. In healthy individuals, these values can vary from 4 to 10 degrees.[9] When increased, PA may be associated with greater amounts of intact cell membranes, indicating adequate health status, whereas low PA values suggest worsening of disease and cell death.[9] PA cutoff points vary between diseases – in HIV-infected patients, a PA lower than 5.3º was associated with a unfavorable prognosis,[32] whereas lower survival rates were found in advanced cancer patients with PA lower than 4.4º.[33]

With respect to HF, Colín-Ramírez et al.[34] investigated a cohort of 389 HF patients in Mexico city and demonstrated that PA is a good prognostic indicator. A PA lower than 4.2º was more strongly associated with mortality (even after adjusting for age), serum hemoglobin and presence of DM. Another study reported a significant reduction in PA values in HF patients as compared with healthy controls (5.5º *vs*. 6.4º).[35]

Colín-Ramirez et al.[34] demonstrated the prognostic value of PA in HF patients, and showed that a lower PA was associated with markers of malnutrition, such as decreased BMI, worsening of functional class and kidney failure.

In the study by Tajeda et al.,[36] a lower PA (4.32º) was associated with changes in glomerular filtration rate and cardiac troponin T levels. Martínez et al.[37] showed that a lower PA was associated with worsening of functional class (from III to IV), even after adjusting for age and sex, and that PA values were significantly lower in patients with preserved systolic function. Colín-Ramírez et al.[38] evaluated patients with systolic and diastolic HF and observed that those with volume overload and anemia had reduced PA values, and such reduction was associated with thyroid disorders in the study by Silva-Tinoco et al.[39]

In the present study, PA had a significant correlation with BMI and a marginal significant correlation with WHtR and LFEV. Therefore, the higher the BMI and WHtR, the higher the PA, indicating that excess weight and body fat could be a protective factor for HF patients, corroborating the results of previous studies on the obesity paradox.[1,4] Besides, the correlation between LVEF and PA supports the use of the latter as a prognostic indicator of HF.

The main limitation of this study was the sample size, as a larger sample size could result in stronger correlations between the variables and yield more definite results.

Conclusion

In our study, most patients had excessive total and central body fat, and correlations of BMI and C-index with WC and WHtR, and of WHtR with WC were found. Besides, there was a trend of correlation of WHtR and LVEF with PA, and a correlation between PA and BMI. We thereby demonstrate a possible example of obesity paradox. Also, we highlight the need for further studies on the use of PA in HFREF, to establish PA cutoff points and enable their application as a prognostic parameter in this population.

Author contributions

Conception and design of the research: Faria TC, Giannini DT, Gasparini PVF, Rocha RM. Acquisition of data: Faria TC. Analysis and interpretation of the data: Faria TC, Giannini DT, Gasparini PVF, Rocha RM. Statistical analysis: Giannini DT. Writing of the manuscript: Faria TC, Giannini DT, Gasparini PVF, Rocha RM. Critical revision of the manuscript for intellectual content: Giannini DT, Gasparini PVF, Rocha RM.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Pesquisa da Universidade do Estado do Rio de Janeiro under the protocol number 47828915.3.0000.5259. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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