

ORIGINAL ARTICLE

Adductor Pollicis Muscle Thickness as a Marker of Nutritional Status in Heart FailureFabiane da Silva Rosário,^{ID} Denise Tavares Giannini,^{ID} Viviane de Oliveira Leal,^{ID} Ricardo Mourilhe-Rocha^{ID}*Universidade do Estado do Rio de Janeiro (UERJ), RJ - Brazil***Abstract**

Background: Malnutrition is associated with morbidity and mortality in patients with heart failure (HF). Thus, it is essential to apply reliable indicators to assess the nutritional status of these individuals.

Objective: To evaluate the thickness of the adductor pollicis muscle (APM) in patients with HF as an indicator of somatic protein status and correlate the obtained values with conventionally used parameters and electrical bioimpedance (EBI) markers.

Methods: Cross-sectional study with patients with HF undergoing regular outpatient treatment. APM thickness was measured in the dominant arm, and the values obtained were classified according to gender and age. The anthropometric parameters assessed included the body mass index (BMI) and specific parameters to assess the muscle (arm muscle circumference [AMC] and arm muscle area [AMA]). Values of phase angle (PA), standard PA (SPA), and lean mass were obtained by EBI. Statistical analyses were performed with the software Statistical Package for the Social Sciences, version 19, using unpaired Student's t, Mann-Whitney, or one-way analysis of variance (ANOVA) tests for comparisons between groups, as appropriate. The correlation between variables of interest was performed using Pearson's or Spearman's correlation coefficient, as adequate. The level of significance was set at 5%.

Results: About 70% of the 74 patients evaluated were classified as malnourished according to the APM thickness. Values of AMC, AMA, and lean mass correlated positively with APM thickness ($p < 0.005$). The APM thickness also correlated positively with PA and SPA ($r = 0.49$, $p < 0.001$ and $r = 0.31$, $p = 0.008$, respectively).

Conclusion: Patients with HF presented a high frequency of protein malnutrition when APM thickness was used as an indicator of nutritional status. APM thickness values correlated with conventional measures of somatic protein evaluation and may be related to the prognosis of these patients, since they correlated positively with PA and SPA. (Int J Cardiovasc Sci. 2018; [online].ahead print, PP.0-0)

Keywords: Heart Failure; Thumb; Malnutrition / mortality; Nutrition Assessment; Anthropometry.

Introduction

A series of neurohormonal modifications, such as chronic inflammation, anorexia, and resistance to anabolic hormones, are common in heart failure (HF) and are closely related to the emergence of malnutrition in this population.^{1,2} Malnutrition, in turn, is associated with a higher prevalence of comorbidities and constitutes an important predictive factor for decreased survival regardless of variables like age, functional class, and ejection fraction (EF).²

Although the classification of nutritional status according to body mass index (BMI) indicates a higher prevalence of eutrophy, overweight, and obesity, when evaluating anthropometric measures specifically used to estimate the muscle compartment, patients with HF commonly present different stages of protein malnutrition, independent of total body mass,^{1,3,4} which can be explained by the fact that BMI does not clearly reflect the body composition.^{5,6}

Dual-energy X-ray absorptiometry is one of the techniques considered the gold standard for assessment

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of body composition; however, difficult logistics associated with its implementation hinders the routine use of this technique in clinical practice. In contrast, electrical bioimpedance (EBI) is considered an alternative and appropriate instrument capable of estimating the body components, distribution of fluids, and cellular quality and integrity.⁷

Anthropometric variables obtained in the upper part of the body, such as the arm muscle circumference (AMC), can also be considered good indicators of somatic protein mass since they are less affected by the presence of edema.⁵ In this sense, the measurement of the thickness of the adductor pollicis muscle (APM) emerges as a promising alternative to evaluate the muscle compartment, since it is a simple, noninvasive, and low-cost method.^{8,9}

The APM is the only muscle in the human body whose thickness can be directly measured without requiring estimating equations, reflecting the loss of working capacity due to limitations from the underlying disease.^{8,9} Due to the lack of scientific evidence on the applicability of APM thickness and its reliability in classifying the nutritional status in individuals with HF, the objective of this study was to evaluate the APM thickness in patients with HF and correlate the results with conventional anthropometric parameters for assessment of the somatic nutritional protein status and with EBI parameters.

Methods

This cross-sectional study evaluated patients regularly attending the Heart Failure Outpatient Clinic at *Hospital Universitário Pedro Ernesto* (HUPE) and was approved by the institution's Research Ethics Committee (HUPE/ UERJ, n. 47828915300005259). All patients were previously informed about the methods and objectives of the study and signed an informed consent form. Considering the absence of data on the average values of APM thickness in patients with HF, standard deviation values for APM thickness found in patients undergoing cardiac surgery⁹ were considered to determine the sample size required for this study. Thus, a minimum of 66 patients would be sufficient to ensure a maximum estimation error of 0.7 mm for APM thickness, with a significance level of 5%.

A total of 90 patients with a diagnosis of HF, of both genders, and aged between 18 and 74 years were considered eligible. The exclusion criteria were patients with clinical evidence of edema and ascites, amputees,

with a pacemaker, or with a BMI < 16 kg/m² or > 34 kg/m², since most equations used to estimate body composition using EBI are unable to predict reliably the body composition in extreme BMI values.¹⁰ Patients were also excluded when failing to follow the standardization protocol for EBI or not using diuretics, resulting in a sample of 74 patients.

The etiology and the HF functional class were defined according to the proposal by the New York Heart Association (NYHA).¹¹ Values of EF were obtained by echocardiography at the moment of the clinical and nutritional evaluation of the patient. The presence of comorbidities was obtained from the patients' clinical records. A patient was considered as having type 2 diabetes mellitus when presenting fasting glucose \geq 126 mg/dL on at least two occasions or using hypoglycemic agents,¹² and as having chronic renal disease when presenting a glomerular filtration rate < 60 mL/min for 3 months.¹³

The assessment of the nutritional status was performed by two previously trained nutritionists and consisted in the assessment of anthropometric measures and EBI.

Anthropometry

Body mass was measured with a mechanical scale (Balmack®, São Paulo, Brazil) with a maximum capacity of 200 kg and subdivisions of 100 grams. Height measurement was obtained with a stadiometer coupled to the scale mentioned above, with an accuracy of 0.1 cm, following the technique proposed by Lohman et al.¹⁴ The nutritional status was assessed according to the BMI, which was classified according to the proposal by the World Health Organization.¹⁵

The technique described by Harrison et al.¹⁶ was used to measure the arm circumference (AC) and triceps skinfold (TSF). The AC was measured on the dominant arm using an inelastic measuring tape. The TSF thickness was measured in triplicate with the adipometer Lange Skinfold Caliper (Cambridge Scientific Industries, Inc., Watertown, MA, USA), with an accuracy of 1 mm, and the mean value of the three measurements was used in the analysis. The AC and TSF values were used to calculate the AMC and arm muscle area (AMA), according to the formulae described by Frisancho.¹⁷ The AMC was classified according to the calculation of the percentage of adequacy in relation to the value corresponding to the 50th percentile according to gender and age, and later compared with the percentages of reference established

by Frisancho.¹⁷ The AMA was directly classified based on the percentiles of reference defined by Frisancho.¹⁸

The APM thickness was measured thrice with the scientific adipometer Lange Skinfold Caliper on the dominant side of the body, in the center of an imaginary triangle formed by the index finger and thumb. During this assessment, the individual remained seated with the hand relaxed and resting on his or her thigh, and the arm positioned so as to form a 90° angle with the forearm.¹⁹ The mean values obtained for the dominant arm were classified according to gender and age, and patients with values below the 5th percentile were considered malnourished. The 5th percentile values are 20, 23, and 18 mm for men in the age range of 18 - 29 years, 30 - 59 years, and above 60 years, respectively. Considering the same age ranges, the 5th percentile values for women are 16, 17, and 14 mm, respectively.²⁰

Electrical bioimpedance

EBI was assessed with the tetrapolar equipment BIA 450 (Biodynamics Corporation, Shoreline, WA, USA) with a 50 kHz sine wave and 800 mA current. The evaluation was performed at the same moment as that of the anthropometric measurements and followed the measurement protocol known as horizontal EBI,²¹ in addition to the criteria proposed by the Brazilian Medical Association.¹⁰

The following EBI parameters were evaluated: phase angle (PA), percentage of body fat (BF), and lean mass. Standard PA values (SPA) were estimated according to the following equation: PA value observed minus the PA reference value according to gender and age, divided by the respective standard deviation.²² Values of PA exceeding 4.2° were considered adequate.²³

Statistical analysis

The distribution of the variables was assessed with the Kolmogorov-Smirnov test, and the data are presented as mean ± standard deviation or median (interquartile range) values, as appropriate. Categorical data are presented as percentage. Comparisons between groups were performed with unpaired Student's t test for parametric variables or Mann-Whitney test for nonparametric variables. One-way analysis of variance (ANOVA) was used to compare parametric variables among three or more groups. The correlation between the variables of interest was

performed using Pearson's or Spearman's correlation coefficients, as appropriate. The significance level was set at 5% ($p < 0.05$), and the statistical analysis was performed using the software Statistical Package for the Social Sciences (SPSS), version 19.0.

Results

A total of 90 patients with HF were considered eligible, of whom 16 (17.7%) were excluded for meeting the exclusion criteria. Of the 74 patients evaluated, most (66.2%) were male and the most frequent etiology of HF was ischemia (28.4%), followed by idiopathic (24.3%), hypertensive (18.9%), alcoholic and infectious (both with 8.1%), and hereditary (5.4%) causes. Chagas' disease and drug use had frequencies of 4.1% and 2.7%, respectively.

Among the patients evaluated, 31 (41.9%) had type 2 diabetes mellitus, 7 (9.5%) had chronic renal disease receiving conservative treatment, and 3 (4.1%) had chronic obstructive pulmonary disease. Approximately 8% of the patients had undergone angioplasty with stent placement. The HF functional class of higher prevalence was NYHA II (40.5%), followed by I (33.8%), III (23.0%), and IV (2.7%). With respect to EF, 88% ($n = 65$) of the patients presented a value below 50%. Only 7% ($n = 5$) of the patients presented PA values below 4.2°. The characteristics of the study population are described in Table 1.

The classification of the nutritional status according to the different nutritional parameters evaluated is presented in Table 2. Most patients presented malnutrition according to the APM thickness, corresponding to approximately 80% ($n = 39$) of the men and 56% ($n = 14$) of the women.

The mean APM values in individuals classified as malnourished and well-nourished were 13.1 ± 3.9 and 18.9 ± 2.9 mm, respectively ($p < 0.0001$, unpaired Student's t test). Patients considered malnourished had lower SPA values when compared with those classified as eutrophic (-0.5 ± 1.42 versus -0.05 ± 1.56 , $p = 0.012$, Mann-Whitney test).

The mean APM thickness values were not different when patients were stratified according to the HF etiology, classification of BMI, AMC or AMA (performed by one-way ANOVA). Also no difference was observed in APM thickness when the patients were stratified by age ($< \text{or} \geq 60$ years, unpaired Student's t test). However, the APM values were higher in patients with NYHA I when

Table 1 - Anthropometric and clinical characteristics of the study population

	Total sample (n = 74)	Men (n = 49)	Women (n = 25)	p value
Age (years)	60 (14.5)	59 (19)	65 (11)	0.012†
APM (mm)	14.8 ± 4.4	15.7 ± 4.0	13.0 ± 4.8	0.015*
EF (%)	35.8 ± 12.3	36.2 ± 13.0	34.9 ± 11.1	0.67*
BMI (kg/m ²)	26.9 ± 3.6	26.8 ± 3.5	27.1 ± 3.9	0.70*
TSF (mm)	21.2 ± 6.1	19.8 ± 4.8	23.8 ± 7.4	0.02*
AMA (cm ²)	45.9 (16.4)	49.8 (13.9)	42.0 (12.1)	0.005†
AMC (cm)	24.0 (4.2)	25 (3.4)	23.0 (3.25)	0.005†
LM (kg)	51.9 ± 10.9	57.3 ± 8.2	41.5 ± 7.6	< 0.001*
BF (%)	30.2 ± 6.9	26.9 ± 5.1	36.8 ± 5.1	< 0.001*
PA (°)	6.4 ± 1.2	6.7 ± 1.1	5.7 ± 1.1	< 0.001*
SPA (°)	-0.30 (1.22)	-0.42 (1.28)	-0.20 (1.27)	0.458†

P values refer to comparisons between men and women. †Mann-Whitney test; *Unpaired Student's t test. APM, adductor pollicis muscle; EF: ejection fraction; BMI: body mass index; TSF: triceps skinfold; AMA: arm muscle area; AMC: arm muscle circumference; LM: lean mass; BF: body fat; PA: phase angle; SPA: standard phase angle.

Table 2 - Nutritional status of patients with heart failure according to assessed nutritional indicators

Parameter	Classification	N (%)
APM	Malnutrition	53 (71.6)
	Eutrophy	21 (28.4)
BMI	Malnutrition	-
	Eutrophy	21 (28.4)
	Pre-obesity	37 (50.0)
	Obesity	16 (21.6)
AMC	Malnutrition	29 (39.2)
	Eutrophy	37 (50.0)
	Overweight/obesity	8 (10.8)
AMA	Severe malnutrition	3 (4.1)
	Mild/moderate malnutrition	7 (9.5)
	Eutrophy	64 (86.5)

AP: adductor pollicis muscle; BMI: body mass index; AMC: arm muscle circumference; AMA: arm muscle area.

compared with those with NYHA II (16.6 ± 4.1 versus 13.7 ± 4.3 mm, *p* = 0.045, unpaired Student's t test). No

significant difference was observed in APM thickness values between groups with EF above and below 50% (unpaired Student's t test).

The APM thickness correlated with the PA, SPA, and anthropometric variables, as shown in Table 3.

Discussion

Protein malnutrition is a frequent condition in patients with HF.^{3,24} Despite the assessment of the APM thickness being considered a useful tool to assess somatic protein status in general,²⁰ its use in the assessment of the nutritional status in patients with HF is still emerging. In this sense, our study was a pioneer in assessing APM thickness in patients with HF and found that about 70% of the patients were considered malnourished when the values of the APM thickness were compared to reference values according to gender and age.

The reduction in muscle mass in patients with HF can be explained by physical inactivity, hypermetabolic status, and drug-nutrient interaction, which leads to symptoms such as anorexia, diarrhea, and intestinal edema which, once present, are responsible for the reduction in food ingestion and absorption of nutrients.¹ In addition, chronic inflammation is closely related to the development of protein depletion in these patients.^{1,2}

Table 3 - Correlations between the thickness of the adductor pollicis muscle and variables of interest

Variables	Total sample (n = 74)		Men (n = 49)		Women (n = 25)	
	R	p value	R	p value	r	p value
BMI	0.28*	0.015	0.29*	0.046	0.34*	0.92
AMC	0.35†	0.003	0.20*	0.16	0.45*	0.02
AMA	0.34†	0.003	0.15†	0.29	0.44†	0.03
LM	0.31*	0.009	0.14*	0.92	0.41*	0.04
PA	0.49*	< 0.001	0.41*	0.003	0.46*	0.02
SPA	0.31†	0.008	0.34†	0.016	0.33†	0.09

*Pearson's correlation coefficient; †Spearman's correlation coefficient. BMI: body mass index; AMC: arm muscle circumference; AMA: arm muscle area; LM: lean mass; PA: phase angle; SPA: standard phase angle.

The APM thickness has been related to mortality and risk of complications in different clinical conditions. Bragagnolo et al.²⁵ observed that the APM thickness was associated with a higher risk of death and postoperative complications in patients undergoing gastrointestinal surgery. In patients undergoing dialysis, APM thickness was demonstrated to be associated with a higher risk of hospitalization during 6 months of follow-up.²⁶ When assessed before cardiac surgery, APM was able to predict clinical outcomes, such as septic complications, length of hospital stay, and mortality.⁹ Although the association between APM and mortality/morbidity has not yet been established for the HF population, the present study demonstrated a direct relationship between APM thickness and PA.

PA is generated from the storage of part of the electric current by the cell membrane,²⁷ and decreased PA values are suggestive of death or reduced cellular integrity, while increased values are suggestive of a greater amount of intact cell membranes. This result is useful even in patients with fluid alteration or in those in whom body weight cannot be measured. In addition, PA values have the advantage of not requiring regression equations, unlike other EBI parameters, such as lean body mass.²⁸

For a healthy population, the mean PA values vary between 4° and 10°, depending on gender and age. Low PA values are related to decreased cellular integrity, reduced lean mass, and increased morbidity and mortality.²⁹ As for an unhealthy population, the cutoff values differ among pathologies. In patients with liver cirrhosis, PA values $\leq 5.4^\circ$ are associated with greater

mortality when compared with patients with PA values greater than these.³⁰ In the same context, studies have identified PA as being a strong prognostic indicator and an important tool to assess clinical signs and monitor disease progression in patients on peritoneal dialysis (PA = 6.0°),³¹ HIV-positive (PA = 5.4°),³² or with lung cancer (PA = 4.5°).³³

Collin-Ramírez et al.²³ also observed in patients with HF that a PA below 4.2° was an independent predictor of mortality. In parallel, patients with PA below this cutoff value (1st distribution quartile) presented lower values of hemoglobin, BMI, and manual dynamometry.

Malnutrition can be detected early by changes in cell membrane and fluid imbalance, which precede anthropometric or biochemical alterations. According to Barbosa-Silva et al.,³⁴ the first level to be affected during the process of malnutrition would be related to metabolic changes, such as alterations in cell membranes detected by PA. Functional muscle changes would be the next affected level, and only after that would anthropometric parameters be modified.

In general, studies show a good correlation between APM thickness and classic anthropometric parameters.^{19,35} Bragagnolo et al.²⁵ observed a positive correlation of APM thickness with BMI, AMC, and TSF in surgical patients. Oliveira et al.,³⁶ when assessing patients on hemodialysis, also found a positive correlation of APM thickness with BMI, AMC, AMA, and PA. An important correlation between APM and lean mass estimated by EBI has also been observed in patients with stroke.³⁵ The present study corroborates these findings, since it showed a correlation

of APM thickness with BMI, AMC, AMA, and lean mass obtained by EBI, especially in women.

Although the present study has observed a correlation between APM thickness and BMI, over half of the patients were classified as having excess weight according to the BMI, and approximately 70% were considered malnourished according to APM thickness. This can be explained by the fact that the BMI is unable to differentiate body compartments, in addition to the fact that increased BMI is associated with a chronic proinflammatory status able to lead to protein depletion.⁶

The APM thickness was also associated with the SPA. The SPA corresponds to the PA adjusted for gender and age from reference values for the Brazilian population.²² Thus, the SPA can be used to compare studies from different populations with different age and gender distributions. The cutoff value of -1.65 represents the 5th percentile and can be considered as the lowest acceptable limit for a healthy population.²⁵ Still, no studies have defined cutoff values for SPA specific to the HF population.

The use of EBI in patients with HF is considered valid by several authors.³⁷⁻³⁹ However, there is still debate about its use in these patients. According to the Brazilian Medical Association,¹⁰ the use of EBI is not appropriate in situations of ionic or fluid imbalance, such as edema and ascites, conditions frequently observed in patients with HF and which promote water retention and increase in extracellular compartment and, therefore, overestimate the fat-free mass,³⁶ a situation highlighted as one of the main sources of error in the application of the method. Martinez et al.⁴⁰ claim that due to the variation in tissue hydration in patients with HF, it would be more appropriate to use "raw measures" generated by EBI, such as reactance, resistance, and PA, since these do not depend on regression equations or the patient's weight.

In the present study, the standardization of assessment using widely known protocols,^{10,21} in addition to the exclusion of patients not using diuretics, maintaining a homogeneous group, and those with clinical evidence of edema and ascites, were essential for better reliability of the EBI results.

When the HF functional classification was assessed, the APM thickness values were observed to be significantly higher in NYHA I patients when compared with NYHA II ones. The NYHA functional classification¹¹ is an instrument with established validity and reliability, used to evaluate the symptomatic effect of cardiac

disease, allowing to stratify the degree of limitation imposed by the disease on daily activities.⁴¹ HF is related to a low tolerance to exercises with pronounced metabolic and respiratory responses capable of leading to inactivity, causing muscle atrophy, which is ultimately associated with fatigue and decreased muscle strength.^{42,43} This way, it is reasonable to propose that the greater the physical limitation, the higher the NYHA functional class¹¹ and, consequently, the lower the somatic protein mass. Therefore, it is possible that the reduction in APM thickness is related to a reduction in daily activities and is independent from the catabolism and the disease itself.⁴³

Although the present study has been a pioneer in evaluating APM thickness as an indicator of nutritional status in patients with HF, it has some limitations. Due to financial and infrastructure limitations, methods that are more accurate in assessing body composition, such as dual-energy X-ray absorptiometry, could not be carried out. Therefore, the sensitivity and specificity of APM thickness compared with the methods considered the gold standard for the evaluation of the somatic nutritional protein status could not be measured. Additionally, the intraobserver and interobserver variability of APM measurements were not evaluated. However, in order to standardize the protocols of assessment and minimize the variability in APM measurements, the nutritionists responsible for the nutritional assessment were previously trained to perform anthropometric assessment and EBI.

Conclusions

The present study showed an increased frequency of malnutrition when APM thickness was used as a diagnostic indicator of nutritional status. Traditional indicators used to categorize the nutritional status were also directly associated with APM thickness. In addition, APM thickness values were directly associated with PA and SPA, recognized prognostic markers in different clinical situations. Additional prospective studies should be conducted in order to evaluate alterations in APM thickness in relation to disease duration and severity, as well as the presence of clinical complications and survival of patients with HF.

Author contributions

Conception and design of the research: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R. Acquisition

of data: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R. Analysis and interpretation of the data: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R. Statistical analysis: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R. Writing of the manuscript: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R. Critical revision of the manuscript for intellectual content: Rosário FS, Giannini DT, Leal VO, Mourilhe-Rocha R.

Potential Conflict of Interest

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

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