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### Original article

# Is there an association between the nutritional and functional parameters and congestive heart failure severity?

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### SUMMARY

*Background & aims:* The association between markers of nutritional status (handgrip strength [HGS] and adductor pollicis muscle thickness [APMT]) and clinical markers of congestive heart failure (CHF) severity is currently unclear. The objective of this study was to evaluate the association between HGS, APMT, as markers of nutritional status and CHF severity.

*Methods:* APMT and muscle strength was measured in 500 CHF patients bilaterally. Nutritional status was assessed by Subjective Global Assessment (SGA). Functional classification was performed according to guidelines provided by the New York Heart Association (NYHA) and ejection fraction (EF) was measured to classify CHF severity. Poisson regression, adjusted for sex and age, was performed to verify the association between nutritional factors and CHF severity markers.

*Results*: The majority of patients (75.8%) were  $\geq$ 60 years old and 53.6% were either overweight or obese. SGA identified 42.2% of the patients as malnourished, 12.6% with low APMT, and 29.0% with low HGS. Most of the patients were classified as NYHA III/IV (56.8%) and almost one third of patients (31.1%) had EF < 40%. HGS and APMT were significantly lower in malnourished male patients and in male patients with a lower EF or worse NYHA classification. Even after controlling for the EF, malnourished patients showed a 2.5-fold increased risk of CHF severity by NYHA classification and for each kilogram of increase in the HGS, there was a significant decrease of 2% in the risk (RR: 0.98 p < 0.001). Malnourished patients presented a 52% higher risk (RR: 1.52 p = 0.016) of having a low EF, whereas for each APMT increase, there was a 5% decrease in the risk (RR: 0.95 p < 0.001), even after controlling for NYHA classification. Conclusions: Malnutrition is highly prevalent among patients with CHF and it is associated with the functional class and the severity of the disease. Objective markers of strength (HGS) and muscle (APMT) are independently associated with the CHF severity, assessed by NYHA classification and EF, respectively, even after adjustment for other confounding variables. Thus, the implementation of these nutritional assessment methods in hospital routines, either by SGA or by objective methods, such as HGS and APMT, can configure effective measurements for early detection of malnutrition in patients at higher risk, and possibly a way to avoid their further functional decline.

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### 1. Introduction

In 2010, almost 38 million people lived with Congestive Heart Failure (CHF) worldwide [1]. CHF is associated with roughly 65,000 deaths in the United States each year [2], and this number is

expected to increase with the prevalence of CHF projected to increase by 46% by the year 2030 [3].

In addition to promoting malnutrition, CHF contributes to the development of cachexia in 15% of patients [4,5]. Therefore, the early evaluation of nutritional status in these patients becomes an important tool for the prevention of the nutritional decline in patients with CHF.

Nutritional assessment using only body measurements, such as body mass index (BMI), may underestimate malnutrition since

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patients with CHF may have fluid retention, and this has great impact in total weight [6,7]. Anthropometric data are frequently used for the nutritional assessment of inpatients, although there is no gold standard that it is completely accurate [8].

The adductor pollicis muscle thickness (APMT) is an important variable to assess the muscle compartment, since it is considered an objective, low-cost, and noninvasive measurement. It has a well-defined anatomical site and it is the only muscle in the human body that allows an almost direct thickness measurement [9,10]. Studies have shown that there is a good correlation of APMT and nutritional status [10,11], as well as an association with the length of hospital stay [11], although its association with clinical outcomes is still controversial [12,13].

Handgrip strength (HGS) is a marker of overall muscle strength, and it has been used as a prognostic marker in several clinical conditions [14].

Together with APMT, HGS may be considered as a marker of muscle mass and function in the nutritional assessment. However, the association between HGS and APMT as markers of muscle function, nutritional status, and clinical outcomes in patients with CHF diagnosis are still not widely discussed in the scientific literature. Furthermore, given the high impact that loss of muscle mass and malnutrition may cause in these patients, the awareness of this association would allow for the implementation of such methods in the clinical investigation for the early identification of patients at higher risk. Thus, this study has the objective of evaluating the association between HGS, APMT, and nutritional status with the severity of the disease in patients with CHF. Our hypothesis is that both APMT and HGS will be associated with the CHF severity, assessed by ejection fraction (EF) and New York Heart Association (NYHA) functional classification.

### 2. Materials and methods

A cross-sectional, observational, prospective study was performed at a reference Cardiology hospital in Rio Grande do Sul state, Brazil, between August 2016 and October 2017. The total number of inpatient service days provided for this period was 11,362. Of these, 1104 had a clinical diagnosis of CHF (signs and symptoms) confirmed by an echocardiogram.

Patients with CHF admitted on Mondays, Wednesdays, and Fridays, aged 18 years of age or older were included in the study. Patients admitted to the Intensive Care Unit, who were candidates for emergency surgery, with a prognosis of survival of less than 90 days, hospitalization shorter than 72 h or who could not perform the anthropometric evaluations and handgrip strength according to the protocol established due to edema or venous access were excluded.

All patients who met the inclusion and exclusion criteria were invited to participate in the study and signed the informed consent form. This study was approved by the Research Ethics Committee of the Institute of Cardiology of Porto Alegre (Brazil), under protocol Up5100/15. According to the sample size estimation, considering the prevalence of malnutrition in hospitalized patients in the region [15] between 33 and 38%, and considering losses and adjustment for confounding factors, a sample of 500 patients diagnosed with CHF were included.

A semi-structured questionnaire was applied to all study participants in order to obtain the following self-reported information: education (in years), marital status, current weight (kg) and height (cm), diagnosis with systemic arterial hypertension (SAH), chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD), and diabetes mellitus (DM).

Body mass index (BMI) was calculated from the referred weight and height  $(kg/m^2)$ . Sex and skin color were observed and recorded by the interviewers.

The socioeconomic status was evaluated according to the criteria of the Brazilian Association of Research Companies (Associação Brasileira de Empresas de Pesquisa - ABEP), which considers the possession of certain consumer goods, the level of education of the head of the family, and the presence of a maid when assessing the socioeconomic status. According to this scale, individuals were considered as the highest (A) to the lowest (E) of the socioeconomic class.

The nutritional assessment was performed through the Subjective Global Assessment (SGA), by two expert professionals in the method. The individuals were classified as nourished (SGA A), suspected of malnutrition or moderate malnutrition (SGA B), or severe malnutrition (SGA C). Patients classified as SGA B or C were considered malnourished in this study.

A single investigator performed the muscle strength assessment and APMT measurement in all patients. Muscle strength was measured at both sides, using a digital manual dynamometer (Jamar Digital Plus + Hand Dynamometer; Simmons Preston, Canada), with the patients seated, with the upper limbs close to the body and the elbow forming a 90° angle [16]. Patients were asked to apply the maximum force they could, three times on each side, and the highest value was considered. The cut points used to identify low strength in the study were  $\leq$ 36.7 kg for men and  $\leq$ 20.8 kg for women younger than 60, corresponding to values below the 5th percentile of the young and healthy local population [17], and  $\leq$ 30 kg for male and  $\leq$ 20 kg for patients older than 60, as established by the European Working Group on Sarcopenia in Older People [18].

The Lange® caliper (Beta Technology, Santa Cruz, CA, USA) was used for the APMT measurement, bilaterally. APMT was pinched with the caliper at the vertex of an imaginary triangle formed by the extension of the thumb and the index finger, with a continuous pressure of 10 g/mm. The mean of three measurements was considered as the APMT. For the analysis, the highest value of APMT between the dominant and the non-dominant limbs was used. APMT values were analyzed comparing the reference values found in the healthy population [19]. Values below the 5th percentile (P5) of the reference values of the local young population, according to sex, were considered low APMT (<17.3 mm for men, and <13.0 mm for women).

Furthermore, to characterize CHF severity, EF information was collected from the electronic medical records. Patients were classified as having a low ejection fraction if they had an ejection fraction equal to or less than 40% or not (heart failure with preserved ejection fraction  $\geq$ 50% and borderline 41–49%) [20]. At the time of the interview, NYHA functional classification was assessed to complete the CHF severity characterization, considering four categories according to the severity of symptoms, from I (lower degree) to IV (higher degree).

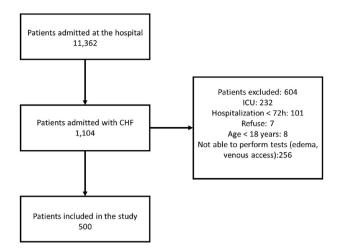
Statistical analysis was performed with statistical software (STATA) 14.0 (StataCorp, CollegeStation,TX,USA). The descriptive analysis of the sociodemographic, anthropometric, nutritional, and clinical characteristics variables was performed initially, as absolute and relative frequency. In the bivariate analysis, mean APMT and HGS values were compared according to nutritional and clinical characteristics. Additionally, a multivariate Poisson regression, adjusted for sex and age, was performed to verify the association (relative risk) of clinical and nutritional factors with CHF severity, considering patients with NYHA functional class III/IV or EF  $\leq$  40% as the highest severity. P-values of equal or less than 0.05 were considered statistically significant for all analyses.

### 3. Results

The flowchart in Fig. 1 describes how the final sample was obtained during the period of the study. A sample of 500 patients was

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**Fig. 1.** Flowchart of the patients included in the study (n = 500).

evaluated, where 50.8% were male, 75.8% were 60 years of age or older, 82.2% were Caucasians, and 47.4% were classified as socio-economic class C (Table 1).

Regarding the nutritional and clinical characteristics of the sample, 53.6% of the patients were classified with some degree of overweight or obesity, considering BMI values, and the prevalence of comorbidities were COPD 11.2%, CRF 13.2%, DM 28.8% and SAH 70%. Moreover, almost half of the sample (42.2% of the patients) presented some degree of malnutrition: 24.4% were classified as moderately malnourished (SGA B), and 17.8% as severely malnourished (SGA C). According to the APMT and HGS values, 12.6% and 29.0% of the CHF patients presented values below the 5th percentile of the healthy population, respectively. When the functional classification from NYHA was evaluated, more than half of the patients (56.8%) belonged to functional classes III and IV. The EF results showed that almost one-third of the patients (31.1%) presented values for EF  $\leq$  40% (Table 2).

The APMT and HGS mean values adjusted by sex are presented in Figs. 2 and 3. These values are lower in malnourished patients and in those with a worse NYHA classification or lower EF, regardless the age. Table 3 shows the HGS mean values (kg) according to nutritional and clinical characteristics by sex and age group. The HGS mean values were significantly lower in all

Table 1
Sociodemographic characteristics of the sample of 500
patients with CHF.

putients that ern:	
Characteristics	n (%)
Sex	
Female	246 (49.2)
Male	254 (50.8)
Age (years)	
18–29.9 years	15 (3.0)
30–59.9 years	106 (21.2)
$\geq$ 60 years	379 (75.8)
Race	
Caucasian	411 (82.2)
Non-caucasian	89 (17.8)
Socioeconomic class	
Α	25 (5.1)
В	202 (41.0)
С	233 (47.4)
D/E	32 (6.5)

CHF: Congestive heart failure; Socioeconomic class: levels A and B are considered the wealthiest, C is middle class, and D and E are the least wealthy. Clinical Nutrition xxx (xxxx) xxx

#### Table 2

Nutritional and clinical characteristics in patients with CHF (n = 500).

$\begin{tabular}{ c c c c } \hline Characteristics & n (%) \\ \hline BMI & & & & \\ <18.5 \ kg/m^2 & 16 \ (3.2) \\ 18.5 \ a 24.9 \ kg/m^2 & 216 \ (43.2) \\ 25 \ a 29.9 \ kg/m^2 & 145 \ (29.0) \\ \ge 30 \ kg/m^2 & 123 \ (24.6) \\ \hline SGA & & & \\ SGA & & & \\ SGA & & & \\ SGA & & & & \\ SGA & & & & \\ SGA & & $
$-18.5 \text{ kg/m}^2$ $16 (3.2)$ $18.5 \text{ a} 24.9 \text{ kg/m}^2$ $216 (43.2)$ $25 \text{ a} 29.9 \text{ kg/m}^2$ $145 (29.0)$ $\geq 30 \text{ kg/m}^2$ $123 (24.6)$ SGASGASGA A $289 (57.8)$ SGA C $89 (17.8)$ APMTAPMTAPMT < $17.3/13.0 \text{ mm}^a$ $437 (87.4)$ APMT < $17.3/13.0 \text{ mm}^a$ $63 (12.6)$
$\begin{array}{cccc} 18.5 & a & 24.9 & kg/m^2 & 216 & (43.2) \\ 25 & a & 29.9 & kg/m^2 & 145 & (29.0) \\ \geq 30 & kg/m^2 & 123 & (24.6) \\ \hline \textbf{SGA} & & & & \\ SGA & & & & & \\ SGA & & & & & \\ SGA & & & & & \\ SGA & & & & & & \\ \textbf{SGA & & & & & \\ SGA & & & & & & \\ \textbf{SGA & & & & & \\ SGA & & & & & \\ \textbf{SGA & & & & & \\ SGA & & & & & \\ \textbf{SGA & & & & \\ SGA & & & & & \\ \textbf{SGA & & & & \\ SGA & & & & & \\ \textbf{SGA & & & & \\ SGA & & & & & \\ \textbf{SGA & & & & \\ SGA & & & & \\ \textbf{SGA & & & & \\ SGA & & & & \\ \textbf{SGA & & & & \\ \textbf{SGA & & & & \\ SGA & & & & \\ \textbf{SGA & & & \\ \textbf{SGA & & & \\ SGA & & & & \\ \textbf{SGA & & & \\ \textbf{SGA & & & \\ \textbf{SGA & & & \\ SGA & & & & \\ \textbf{SGA & & \\ \textbf{$
$\begin{array}{cccc} 25 a & 29.9 \ \text{kg/m}^2 & 145 \ (29.0) \\ \geq 30 \ \text{kg/m}^2 & 123 \ (24.6) \\ \hline \text{SGA} & & & \\ $
≥30 kg/m <sup>2</sup> SGA SGA 289 (57.8) SGA 289 (57.8) SGA C 89 (17.8) APMT APMT 437 (87.4) APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
SGA         289 (57.8)           SGA A         289 (57.8)           SGA B         122 (24.4)           SGA C         89 (17.8)           APMT            APMT < 17.3/13.0mm <sup>a</sup> 437 (87.4)           APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
SGA A       289 (57.8)         SGA B       122 (24.4)         SGA C       89 (17.8)         APMT       437 (87.4)         APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
SGA B       122 (24.4)         SGA C       89 (17.8)         APMT       437 (87.4)         APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
SGA C $89 (17.8)$ APMT $437 (87.4)$ APMT < $17.3/13.0$ mm <sup>a</sup> $63 (12.6)$
APMT         437 (87.4)           APMT ≥ 17.3/13.0mm <sup>a</sup> 437 (87.4)           APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
APMT ≥ 17.3/13.0mm <sup>a</sup> 437 (87.4)           APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
APMT < 17.3/13.0mm <sup>a</sup> 63 (12.6)
HGS
Normal 355 (71.0)
Low <sup>b</sup> 145 (29.0)
NYHA
I 67 (13.4)
II 149 (29.8)
III 125 (25.0)
IV 159 (31.8)
Ejection Fraction
>40% 344 (68.9)
$\leq 40\%^{c}$ 155 (31.1)

CHF: Congestive heart failure; BMI: Body Mass Index; SGA: Subjective Global Assessment; SGA A: Well-nourished; SGA B: Suspected or moderately malnourished; SGA C: malnourished; APMT: Adductor Pollicis Muscle thickness; HGS: handgrip strength; NYHA: Congestive heart failure functional class according to New York Heart Association.

<sup>a</sup> APMT: adductor pollicis muscle thickness values for 5th percentile of reference population.

<sup>b</sup> Low HGS: < 60 years:  $\le 36.7$  kg (male) and  $\le 20.8$  kg (female);  $\ge 60$  years:  $\le 30$  kg (male) and  $\le 20$  kg (female).

<sup>c</sup> Patients with preserved ejection fraction (>50%) and borderline preserved ejection fraction (41%–49%) were considered as a only group: no-reduced ejection fraction.

malnourished males, but only in the older malnourished females when compared to those considered nourished. The same result was observed regarding NYHA functional class: a significantly lower HGS were found in all males with higher dysfunction (Class III/IV), but only older females, when compared to those with functional classes I/II. When the EF was evaluated, it was observed that only males with low EF values, regardless of age, showed significantly lower HGS values when compared to those with normal EF.

Table 4 shows the APMT values (mm) according to the nutritional and clinical characteristics by sex and age group. It was observed that malnourished patients had significantly lower APMT values than the nourished ones, regardless of age or sex. When APMT values were evaluated according to the functional class and EF, it was observed that APMT values were significantly lower in patients with functional class III/IV and EF  $\leq$  40%, than those with class I/II and EF >40%, respectively, regardless of sex and age group.

When the factors associated with functional class III and IV (Table 5) were evaluated through the Poisson multivariate analysis adjusted for sex and age, it was observed that, even after adjustment for the EF, nutritional status and HGS remained as factors associated with a worse functional impairment assessed by NYHA classification. Patients with EF  $\leq$  40% presented a 30% higher risk of a worse functional impairment (class III/IV) (RR:1.30, 95%CI:1.16; 1.47, p < 0.001).

Regarding the nutritional characteristics, it was verified that malnourished patients (SGA B and C) showed a 2.5-fold increased risk of having functional impairment and for each extra kilogram in

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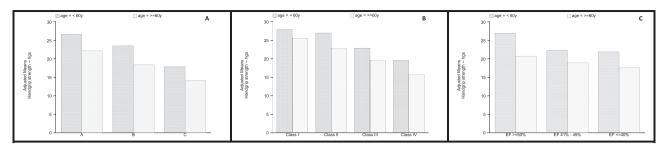


Fig. 2. Handgrip strength mean values (adjusted by sex) according to age and nutritional status (A), NYHA functional classification (B) or ejection fraction (C).

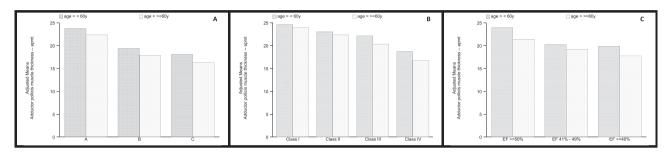


Fig. 3. Adductor pollicis muscle thickness mean values (adjusted by sex) according to age and nutritional status (A), NYHA functional classification (B) or ejection fraction (C).

## Table 3 Handgrip strength values (kg) according to the nutritional and clinical characteristics, sex, and age in patients with CHF.

Characteristics	Female		Male	
	<60 y	≥60 y	<60 y	≥60 y
SGA	p = 0.252	p < 0.001	p = 0.003	p < 0.001
SGA A	$20.0 \pm 5.5$	$16.7 \pm 5.6$	33.5 ± 11.3	$27.2 \pm 8.2$
SGA B/C	$18.1 \pm 4.3$	$12.3 \pm 5.3$	$23.5 \pm 8.8$	$20.5 \pm 8.1$
NYHA	p = 0.078	p < 0.001	p < 0.001	p < 0.001
I/II	$20.3 \pm 4.9$	$17.9 \pm 5.2$	34.9 ± 1.9	$28.3 \pm 7.5$
III/IV	$17.7 \pm 6.0$	$13.1 \pm 5.6$	$24.5 \pm 1.9$	$21.2 \pm 8.5$
Ejection Fraction	p = 0.134	p = 0.078	p = 0.027	p = 0.016
>40%	$20.1 \pm 5.6$	$14.7 \pm 5.8$	33.3 ± 11.2	$25.6 \pm 8.0$
${\leq}40\%$	17.6 ± 3.8	$13.0 \pm 5.9$	26.3 ± 11.0	$22.4 \pm 9.8$

CHF: Congestive heart failure; SGA: Subjective Global Assessment; NYHA: Congestive heart failure functional class according to New York Heart Association. Results were showed as mean  $\pm$  standard deviation and p values are from t test comparing HGS values between variables categories in the same age and sex group.

### Table 4

Adductor pollicis muscle thickness values (mm) according to the nutritional and clinical characteristics, sex, and age in patients with CHF.

Characteristics	Female		Male	
	<60 y	≥60 y	<60 y	≥60 y
SGA	p = 0.001	p < 0.001	p < 0.001	p < 0.001
SGA A	$21.3 \pm 4.2$	$20.2 \pm 3.4$	$26.1 \pm 3.9$	$24.5 \pm 4.0$
SGA B/C	17.9 ± 3.2	$15.4 \pm 3.6$	$20.3 \pm 19.1$	$18.9 \pm 4.3$
NYHA	p = 0.048	p < 0.001	p < 0.001	p < 0.001
I/II	$21.2 \pm 4.4$	$19.8 \pm 3.0$	$26.4 \pm 4.0$	$25.1 \pm 3.8$
III/IV	18.8 ± 3.8	$16.7 \pm 4.3$	$21.8 \pm 3.4$	$19.7 \pm 4.4$
Ejection Fraction	p = 0.007	p < 0.001	p < 0.001	p < 0.001
>40%	$21.2 \pm 4.2$	$18.4 \pm 4.3$	$26.0 \pm 4.2$	$23.4 \pm 4.9$
${\leq}40\%$	$17.6 \pm 3.9$	$15.5 \pm 3.4$	$22.1 \pm 3.6$	19.8 ± 4.2

CHF: Congestive heart failure; SGA: Subjective Global Assessment; NYHA: Congestive heart failure functional class according to New York Heart Association. Results were showed as mean  $\pm$  standard deviation and p values are from t test comparing HGS values between variables categories in the same age and sex group.

### Table 5

Multivariable analysisa of risk factors for	functional c	class III/IV (	(NYHA) in 500	) pa-
tients with CHF.				

	RR	CI 95%	p value
Ejection Fraction			
>40%	1		< 0.001
$\leq$ 40%	1.30	1.16; 1.47	
SGA classification			
SGA A	1		< 0.001
SGA B or C	2.48	2.01; 3.05	
HGS (kg)	0.98	0.97; 0.99	< 0.001

CHF: Congestive heart failure; NYHA: Congestive Heart Failure Functional class according to New York Heart Association; RR: Relative Risk; CI: confidence interval; SGA: Subjective Global Assessment; HGS: handgrip strength. <sup>a</sup> Poisson regression adjusted to sex and age.

HGS there was a significant decrease of 2% in the risk of having a functional impairment (RR: 0.98, 95%CI:0.97; 0.99, p < 0.001).

When the factors associated with low EF (Table 6) were evaluated through the Poisson multivariate analysis adjusted for sex and age, it was found that patients classified as NYHA functional class III/IV, as expected, had a three-fold increased risk of also having a low EF. It was observed that even after adjustment for functional class, both nutritional status and APMT remained as factors significantly associated with a worse ventricular function. Regarding the nutritional variables, the malnourished patients presented a 52% higher risk of having low EF (RR: 1.52, 95%CI:1.08; 2.15, p = 0.016), whereas there was a 5% decrease in the risk of having low EF (RR:0.95, 95%CI:0.92; 0.98, p < 0.001) for each one mm addition of APMT.

### 4. Discussion

In this study, we were able to demonstrate that malnutrition is highly prevalent in patients with CHF, and that there is an association between the nutritional status and the severity of the disease,

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#### Table 6

Multivariable analysis a of risk factors for reduced ejection fraction (EF  $\leq 40\%$ ) in 500 patients with CHF.

RR	CI 95%	p value
1		< 0.001
3.01	1.88; 4.82	
1		0.016
1.52	1.08; 2.15	
0.95	0.92; 0.98	0.001
	1 3.01 1 1.52	1 3.01 1.88; 4.82 1 1.52 1.08; 2.15

CHF: Congestive heart failure; RR: Relative Risk; CI: confidence interval; NYHA: Congestive Heart Failure Functional class according to New York Heart Association; SGA: Subjective Global Assessment; APMT: adductor pollicis muscle thickness. <sup>a</sup> Poisson regression adjusted to sex and age.

as assessed by SGA or function and muscle markers (HGS, APMT). Significantly lower APMT values were found in all patients considered malnourished, with higher dysfunction (NYHA III/IV), and with low EF. A different result was found when the function marker (HGS) was evaluated. Significant lower HGS values were also found in male patients considered malnourished, with higher dysfunction (NYHA III/IV), and with a low EF, but only older female patients who were considered malnourished and with higher dysfunction (NYHA III/IV) showed significant lower strength as assessed by HGS.

The prevalence of malnutrition in patients with CHF can vary from 12 to 69%, depending on the method used for nutritional assessment [21]. A high prevalence of malnutrition (43.1%) in patients with CHF was also found in another study that used the CONUT Score for nutritional evaluation [22]. Such higher prevalence is similar to the one we have found in the present study (42.2%), although nutritional status was assessed employing different methods and parameters. We used the SGA in the present study, which is a subjective and widely accepted nutritional assessment method. In contrast, the CONUT Score used only laboratory parameters, expressing more the inflammatory component (prognosis) associated with malnutrition than the nutritional status [23].

As there is no consensus on the best method of nutritional assessment for patients with CHF, BMI is used in many studies as a nutritional status marker. A recent meta-analysis of sixty papers correlating nutritional status with HF using BMI demonstrated the presence of the obesity paradox, where obese patients with HF achieve a more prolonged survival than non-obese patients [21]. It is known that BMI is not a good marker of adiposity or body composition, and it should not be used individually, without other anthropometric or clinical parameters, as a single marker of malnutrition or obesity [21].

Only two studies with patients with HF assessed by BMI showed a higher severity of symptoms (functional class III and IV) in obese patients [24,25]. Although the present study also used BMI, only malnutrition identified by SGA remained as a significant risk factor associated with higher severity of the disease after adjustment for confounding factors. These findings reinforce the idea that malnutrition identified by BMI is not a good prognostic marker in this population.

This study showed an association between malnutrition and worse ventricular function and functional class. One of the possible explanations for this association would be iron deficiency, commonly found in malnourished patients. A recent study showed that iron deficiency may affect skeletal muscle functioning and can contribute to skeletal myopathy seen in patients with HF [26].

The relationship between malnutrition, HF severity, and negative outcomes may vary depending on how malnutrition is defined. Weight loss is another key criterion for malnutrition diagnosis, usually associated with a worse prognosis. Nonetheless, its role as a risk factor for negative outcomes in patients with HF is not uniform [27]. Regarding the association of weight loss and mortality, it was shown that weight loss is a predictor of higher mortality only in non-obese no-diabetic patients, with no unfavorable impact in patients with Diabetes Mellitus or obesity [27].

Significantly lower values of APMT were found in all malnourished patients, with more significant dysfunction (NYHA III/IV) and with low EF, regardless of the age group or sex. The decrease in APMT found in these patients may reflect a marked general loss of muscle mass in these patients. This loss could be the result of adaptive changes in the musculoskeletal system after the occurrence of CHF. Such muscle changes play an essential role in the development of many symptoms related to heart failure syndrome, including exercise intolerance and fatigue [5,28,29]. In this sense, the APMT measure would be efficient in its detection. Patients with systolic congestive heart failure may experience muscle fiber atrophy, myocytic apoptosis, and increased interstitial inflammatory cells [30]. These deficiencies are able to not only justify the loss of muscle mass, but also to justify the impaired function, as shown in this study.

Concerning HGS, we have found different results according to sex: significant lower HGS values were found in all malnourished males, with greater dysfunction (NYHA III/IV) and with low EF, while a lower HGS was found only in older females with malnutrition or those with higher dysfunction (NYHA III/IV). These results can be justified by the fact that in males, the decline in muscle function occurs more gradually, while in females, a sudden loss of muscle mass and function after menopause is more common [31]. The reduction in skeletal muscle strength may occur due to the low intake of nutrients and hypermetabolism present in patients with HF [32].

Muscle weakness can also be a result of a disruption in the immune system function, mainly due to malnutrition, and mostly because of an insufficient supply of proteins and energy. The weakening of the integrated functions of protective barriers can result in frequent infections, which, along with a decrease in cardiac output, increases the risk of worsening HF and decreases survival at any level of cardiac function [32,33]. Also, malnutrition in patients with HF may be associated with increased edema, inflammatory reactions, and complications [33,34]. In this sense, the use of methods for the early detection of malnutrition in patients with HF allows for the development of interventions, all of which can be associated with a better prognosis for the patients [33–35].

One of the major limitations of the present study was that CHF severity was assessed only by NYHA functional classification and EF. Other biochemistry markers (brain natriuretic peptide [BNP] levels and others) would be more sensitive to characterize the CHF severity. However, these tests are not part of the patient's assessment routine, and it would determine a larger number of missing patients due to incomplete assessments. Another limitation was that it was conducted in only one hospital for the pathology studied. Nevertheless, a representative sample of these patients was evaluated by a single investigator, using instruments with proven reliability and specificity, thus guaranteeing the standardization of the method and the quality of the results. This study also did not discuss the different underlying etiologies of CHF, considering that they might be more related to the clinical aspects of the disease. Our main objective was to understand the relationship between the functional parameters (EF and NYHA classification), regardless of the etiology, and the nutritional aspects assessed by HGS and APMT.

Since this was a transversal study, we could not establish a causal relationship between the nutritional status and the severity of the disease. However, longitudinal studies could show if early

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nutritional intervention and improvement of nutritional parameters could help to improve the functional status and severity of the disease. Recent literature lacks studies evaluating APMT and HGS in nutritional intervention studies in patients with CHF. Thus, further studies are needed to better understand the causal relationship between the clinical and the nutritional parameters in patients with this pathology and to verify the impact of nutritional intervention on the clinical evolution of these patients.

In conclusion, patients with CHF had a high prevalence of malnutrition when assessed by SGA. Also, low APMT and HGS values were associated with poorer nutritional status and worse functional and clinical status, as demonstrated by NYHA and EF classification.

Thus, the implementation of these nutritional assessment methods in hospital routines, either by SGA or by objective methods, such as HGS and APMT assessments, can be efficient measurements for the early detection of malnutrition and patients at higher risk. Appropriate nutritional interventions in these higher-risk patients may improve their prognosis.

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### Statement of authorship

The study was designed by RRPD and MCG. Data collection was conducted by RRPD and MRG. Data analysis was conducted by RRPD and MCG, and interpretation was conducted by RRPD, MCG, and IC. The first draft of the manuscript was prepared by RRPD and MCG. All authors participated in subsequent revisions and approved the final manuscript version. All authors agree that they are accountable for the accuracy and integrity of the work.

### Conflict of interest

The authors have no conflict of interest to declare.

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