

Original article

Malnutrition syndrome, but not body mass index, is associated to worse prognosis in heart failure patients

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SUMMARY

Background & aims: Many studies have suggested that obese patients with chronic heart failure have a better prognosis than leaner patients. The main purpose of this study was to assess the prognostic value of body mass index in patients with chronic heart failure, independently of other poor prognosis parameters.

Methods: This retrospective study included 405 heart failure patients. Anthropometric, body composition, clinical, biochemical, and echocardiographic data were collected from all patients. Patients were classified as: *underweight* (<20 kg/m²), *normal* (20–24.9 kg/m²), *overweight* (25–29.9 kg/m²), and *obese* (≥30 kg/m²). The endpoints were all-cause and cardiovascular mortality.

Results: Cox regression analysis on all-cause mortality showed that normal weight patients were at significantly lower risk of death [RR = 0.231 (CI_{95%} 0.085–0.627)] as compared with obese patients, while underweight and overweight categories did not show a significantly different risk compared with the reference category. Age, gender, ejection fraction, systolic heart failure, angiotensin II receptor blockers use, hemoglobin levels, and handgrip strength were independent predictors of all-cause mortality. Cardiovascular deaths showed the same trend.

Conclusion: A lower body mass index does not predict all-cause and cardiovascular mortality among chronic heart failure patients, independently of other nutritional, body composition, and clinical status parameters.

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1. Introduction

Obesity has been recognized as an important risk factor for the development of cardiovascular disease (CVD)¹ and chronic heart failure (CHF).² However, during the last decade many studies^{3,4} have suggested that obese patients with CHF have a better prognosis than leaner patients, which is referred as the “obesity

paradox”. Several explanations for this association have been proposed.^{3,5}

Most studies observing this “paradoxical” association have used body mass index (BMI) to classify obesity. However, even when BMI is considered a surrogate for obesity, it does not discriminate between fat and lean mass. A recent study of Oreopoulos et al.⁶ that incorporated lean mass in the model to examine the association between body composition and CHF prognostic factors, found that a higher lean body mass and/or lower fat mass was independently associated with factors that are prognostically advantageous in CHF. These results suggested that differentiating between body fat and lean body mass may explain some of the apparently paradoxical associations between BMI and prognosis in heart failure (HF). However, they not evaluate survival or adjust for other parameters of body composition such volume overload, which is common in CHF patients and reflects a greater severity of the disease, due to an overexpression of inflammatory state, contributing to a worse prognosis.^{7–9}

Abbreviations: CVD, Cardiovascular disease; CHF, Chronic heart failure; BMI, Body mass index; HF, Heart failure; INCMNSZ, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; BIA, Bioelectrical impedance analysis; R, Resistance; Xc, Reactance; BIVA, Bioelectrical impedance vectorial analysis; ECW, Extracellular water; LVEF, Left ventricular ejection fraction; ARBs, Angiotensin II receptor blockers; BNP, Brain natriuretic peptide; (VO₂), Ventilatory oxygen uptake.

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The underlying hypothesis of this study was that patients with lower BMI are suffering of a severer HF and a malnutrition syndrome^{5,10} related to it. Therefore, the main purpose of this study was to assess the prognostic value of BMI in patients with CHF, independently of other parameters of nutritional status, body composition and poor prognosis.

2. Materials and methods

2.1. Study population

A total of 405 patients attended to the Heart Failure Clinic of the “Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán” (INCMNSZ) in Mexico City, were studied retrospectively. Patients were included if they were 18 y or older, with confirmed diagnosis of HF (defined as decreased systolic and/or diastolic function as determined by echocardiogram),¹¹ and with follow up of 3 y at the Heart Failure Clinic. Subjects were excluded if they had uncontrolled dysthyroidism, hepatic failure, suspicion of tumoral activity, or limb amputations.

Once incorporated to the Heart Failure Clinic, anthropometric, body composition, clinical (including exercise testing), biochemical, and echocardiographic evaluations were performed in all patients. Exercise testing, biochemical, and echocardiographic evaluations were performed within three weeks of the initial referral; patients with later or incomplete evaluations were excluded from the analysis. All data were taken from the Heart Failure Clinic Registry and from medical records. The present study was approved by the Institutional Ethics Committee of Biomedical Research in Humans of the INCMNSZ.

2.2. Anthropometry

Weight and height were measured according to the reference manual of anthropometric standardization,¹² and all subjects wore little clothing and were barefoot. BMI was calculated by dividing total body weight (kilograms) by height squared (square meters). Patients were classified into three BMI categories: *underweight* (<20 kg/m²), *normal* (20–24.9 kg/m²), *overweight* (25–29.9 kg/m²), and *obese* (≥30 kg/m²).

2.3. Body composition

It was evaluated by the bioelectrical impedance analysis (BIA). Whole-body bioelectrical impedance was measured using a tetrapolar and multiple-frequency equipment (BodyStat QuadScan 4000, Bodystat Ltd.; Isle of Man, UK). Measurements were made by standardized nutritionist according to the tetrapolar method reported in the existing literature.¹³ Subject should be fasting and should not have exercised or taken a sauna 8 h before the study, and should not have consumed alcohol 12 h before the study. The impedance values were obtained at frequencies of 5, 50, 100, and 200 kHz.

Using the standard 50-kHz frequency, resistance (R) and reactance (Xc) were obtained by the Phase Angle Software 1.0 (Bodystat Ltd.) These data, standardized by height, were processed by the bioelectrical impedance vectorial analysis (BIVA)^{14,15} to determine the presence of a *cachectic status*, defined as an individual subject vector fell on or outside of the lower right quadrant of the 95% tolerance ellipse in the RXc graph, using the bivariate, gender-specific, 50%, 75%, and 95% tolerance limits of the impedance vector in a Mexican reference healthy population.¹⁶ So, a cachectic status by this method is characterized by a vector displacement downward to the right along the minor axis of the RXc graph, indicating less cell mass.¹⁷

Extracellular water (ECW), as percentage of total body weight, was also obtained by a modeling program supplied by the manufacturer of the analyzer using a 5 kHz signal. This estimation has been used in patients with varying degree of fluid retention, such as surgical¹⁸ and critically ill¹⁹ patients, in which, the method showed a good reproducibility for fluid measurements and a good correlation with values obtained from radioisotope dilution and deuterium measurement, respectively. In addition, an independent panel of BIA experts in 1997 recommended the utilization of multifrequency BIA in estimating ECW even in the presence of altered fluid distribution.²⁰

Percentiles were constructed for this variable and patients were classified as with an important *fluid retention* if they were on or above the 95th percentile for each gender.

2.4. Clinical data

Functional class according the New York Heart Association (NYHA)²¹ were evaluated during the medical interview. Functional capacity was measured in metabolic equivalents (METs) with symptom-limited treadmill exercise testing, conducted according to Bruce modified protocol. In addition, all patients underwent a transthoracic echocardiogram to determine ventricular function. Medication and co-morbidities were also collected.

2.5. Nutritional status

Fasting plasma *hemoglobin* concentrations were collected and *handgrip strength* was measured using the Smedley Hand Dynamometer (Stoelting, Wood Dale, UK). Patients were instructed to apply as much handgrip pressure as possible by using their dominant hand. The measurements were repeated twice, and the highest score was recorded in kilograms.

2.6. Endpoints

The primary endpoint of this study was all-cause mortality. Survival status after three years of follow up was obtained from the Heart Failure Clinic Registry and from medical records. As secondary endpoint, cardiovascular deaths (sudden, progressive HF, cardiac arrhythmias, stroke, or myocardial infarction) were analyzed.

2.7. Statistic analysis

All analyses were performed with commercially available software (SPSS 15.0 for Windows, SPSS, Inc., Chicago, IL, USA). Continuous variables are expressed as mean ± standard deviation, and categorical variables are presented as absolute and relative frequencies. For the comparison between BMI groups on continues variables one-way analysis of variance (ANOVA) was used, and for categorical variables Pearson chi-squared test. A post hoc analysis with the Bonferroni method was performed for continuous variables, with $p < 0.05$ in simple comparison (ANOVA). Kaplan–Meier survival analysis with Log rank significance test was also performed. Multivariate analysis was performed by Cox proportional hazards regression analysis to estimate adjusted relative risks (RR) and 95% confidence intervals for potential predictors of death. The Cox model included variables found to be statistically different in the bivariate comparisons between BMI groups, and the category of BMI defined as “obese” was considered as the reference category for this analysis. A P -value < 0.05 was considered statistically significant.

3. Results

Of the 405 included patients, 26 (6.4%), 114 (28.2%), 133 (32.8%), and 132 (32.6%) were classified as underweight, normal, overweight, and obese, respectively. The baseline characteristics of the study population according BMI categories are listed in Table 1. Underweight patients had a higher proportion of individuals with cachexia, fluid retention (percentage of ECW $\geq$ 95th percentile), and systolic HF; as well as less mean handgrip strength, hemoglobin level, and left ventricular ejection fraction (LVEF), also a lower use of angiotensin II receptor blockers (ARBs). Renal failure frequency was higher among patients with normal BMI, and overweight patients were more likely to be older and to have dyslipidemia and ischemic etiology; whereas those with obesity had a higher proportion of individuals with hypertension and diabetes. The rest of the clinical variables and medication were not significantly different among groups.

During the three years of follow-up, 70 deaths occurred. Of this, 33 were cardiovascular and 37 were from other (21) or unknown (16) causes. Kaplan–Meier survival analysis among BMI categories showed the worst survival for underweight patients at three years, for both all-cause (Fig. 1) and cardiovascular deaths (Fig. 2). Obese and normal weight patients had a better survival for all-cause and cardiovascular mortality, respectively.

When Cox regression analysis on all-cause mortality (Table 2) was performed, considering as covariates those variables that were

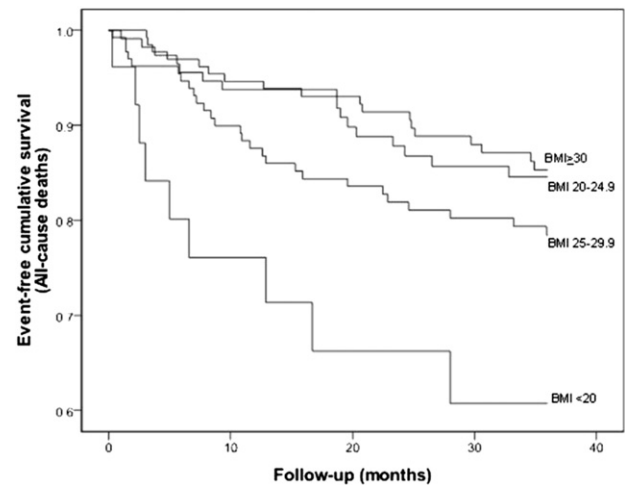


Fig. 1. Kaplan–Meier survival curves at three years for all cause deaths.

statistically different in the bivariate analysis [age, gender, LVEF, systolic HF, ischemic etiology, hypertension, renal failure, dyslipidemia, ARBs use, hemoglobin levels, handgrip strength, fluid retention (extracellular water $\geq$ 95th percentile), and cachexia], normal weight patients were at significantly lower risk of death [RR = 0.231 (CI_{95%} 0.085–0.627)] as compared with obese patients,

Table 1

Baseline characteristics of study population according to body mass index category^a.

	BMI < 20 kg/m ² n = 26	BMI 20–24.9 kg/m ² n = 114	BMI 25–29.9 kg/m ² n = 133	BMI $\geq$ 30 kg/m ² n = 132	p Value between groups ^b
Male	6 (23.1)	64 (56.1)	81 (60.9)	67 (50.8)	0.004
Age (y)	56.6 $\pm$ 20.5	58.3 $\pm$ 22.4	63.3 $\pm$ 14.8	62.3 $\pm$ 13.3	0.57
Body Mass Index (kg/m ²)	18.7 $\pm$ 0.8	22.8 $\pm$ 1.3 ^{d,i}	27.5 $\pm$ 1.4 ^{e,i}	35.7 $\pm$ 5.5 ^{f,i}	<0.0001
Cachexia ^c	18 (69.2)	61 (53.5)	60 (45.1)	30 (22.7)	<0.0001
Extracellular water (%)	28.0 $\pm$ 2.4	26.1 $\pm$ 2.5 ^{d,i}	23.6 $\pm$ 2.1 ^{e,i}	21.0 $\pm$ 2.0 ^{f,i}	<0.0001
Extracellular water $\geq$ 95th percentile	7 (26.9)	8 (7.0)	2 (1.5)	0 (0.0)	<0.0001
Handgrip strength (kg)	13.5 $\pm$ 8.9	20.1 $\pm$ 8.4 ^{d,g}	21.8 $\pm$ 9.6 ^{e,h}	24.2 $\pm$ 11.8 ^{f,i}	<0.0001
Hemoglobin (g/dL)	12.9 $\pm$ 2.6	13.0 $\pm$ 2.6	13.7 $\pm$ 2.4	14.6 $\pm$ 2.2 ^{f,g}	<0.0001
Systolic heart failure	18 (69.2)	50 (43.9)	65 (48.9)	42 (31.8)	0.001
NYHA functional class					
I	11 (42.3)	65 (57.0)	71 (53.4)	53 (40.2)	NS
II	12 (46.2)	31 (27.2)	44 (33.1)	56 (42.4)	
III	3 (11.5)	18 (15.8)	18 (13.5)	23 (17.4)	
Left ventricular ejection fraction (%)	34.5 $\pm$ 16.4	42.3 $\pm$ 16.1	43.6 $\pm$ 15.8	48.7 $\pm$ 15.5 ^{f,i}	<0.0001
Functional capacity (mets)	5.0 $\pm$ 2.3	5.9 $\pm$ 3.9	5.8 $\pm$ 3.3	6.5 $\pm$ 3.2	NS
Ischemic cardiomyopathy	10 (38.5)	51 (44.7)	80 (60.2)	55 (41.7)	0.011
Hypertension	13 (50.0)	75 (65.8)	98 (73.7)	108 (81.8)	0.002
Diabetes	9 (34.6)	49 (43.0)	62 (46.6)	71 (53.8)	NS
Dyslipidemia	8 (30.8)	66 (57.9)	98 (73.7)	95 (72.0)	<0.0001
Dysthyroidism	8 (30.8)	26 (22.8)	23 (17.3)	35 (26.5)	NS
Renal Failure	4 (15.4)	44 (38.6)	26 (19.5)	15 (11.4)	<0.0001
History of malignance	2 (7.7)	7 (6.1)	13 (9.8)	9 (6.8)	NS
Beta-blockers	22 (84.6)	97 (85.1)	112 (84.2)	105 (79.6)	NS
ARBs	12 (46.2)	74 (64.9)	78 (58.6)	94 (71.2)	0.04
ACEIs	13 (50)	37 (32.5)	49 (36.8)	43 (32.6)	NS
Diuretics	16 (61.5)	75 (65.8)	94 (70.7)	101 (76.5)	NS
Digitalis	14 (53.8)	55 (48.2)	55 (41.4)	48 (36.4)	NS
Oral nitrate	7 (26.9)	32 (28.1)	53 (39.8)	34 (25.8)	NS
Aldosterone receptor antagonists	17 (65.4)	68 (59.6)	77 (57.9)	75 (56.8)	NS
Aspirin	2 (7.7)	19 (16.7)	23 (17.3)	16 (12.1)	NS

Abbreviations: NYHA, New York Heart Association; ARBs, angiotensin II receptor blockers; ACEIs, Angiotensin-converting enzyme inhibitors; NS, not significant.

^a Categorical values are No. (percentage) of patients, and continuous values are mean $\pm$ SD.

^b By one-way analysis of variance for continuous variables and Pearson chi-squared test for categorical variables.

^c Subjects with an impedance vector on or outside of the lower pole of the 95% tolerance ellipse in the right side of the gender-specific RXc graph.

^d Difference between BMI < 20 kg/m² and BMI 20–24.9 kg/m² categories.

^e Difference between BMI < 20 kg/m² and BMI 25–29.9 kg/m² categories.

^f Difference between BMI < 20 kg/m² and BMI $\geq$ 30 kg/m² categories.

^g Statistically significant difference at $p < 0.05$.

^h Statistically significant difference at $p < 0.01$.

ⁱ Statistically significant difference at $p < 0.001$.

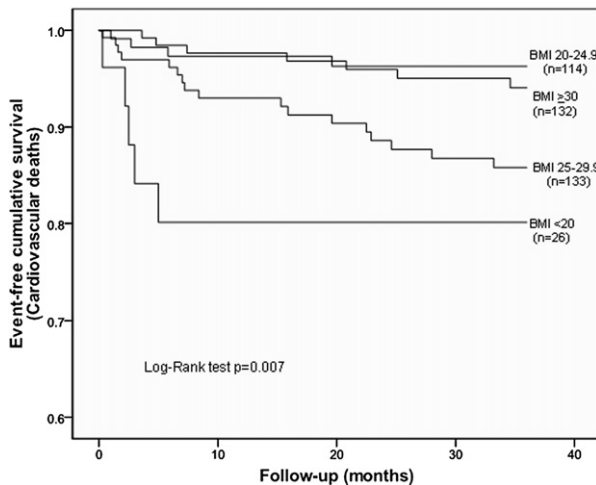


Fig. 2. Kaplan–Meier survival curves at three years for cardiovascular deaths.

while underweight and overweight categories did not show a significantly different risk compared with the reference category. In this model, age, gender, LVEF, systolic HF, ARBs use, hemoglobin levels, and handgrip strength were independent predictors of all-cause mortality.

When cardiovascular deaths were analyzed, BMI categories showed the same trend, with a lower risk for normal weight patients [RR = 0.102 (CI_{95%} 0.021–0.498)] compared with those obese. All independent predictors for all-cause mortality were remained for cardiovascular deaths (Table 3).

4. Discussion

In this longitudinal study in patients with CHF, it was found that a lower BMI (<20 kg/m²) was associated with characteristics agree with a less favorable body composition, nutritional, and clinical status, since patients within this BMI category had the highest proportion of individuals with cachexia, fluid retention, and

Table 2
Multivariate predictors of all-cause mortality in the study population (Cox proportional hazard regression analysis).

	<i>B</i> ^a	RR ^b	95% CI for RR	
			Lower	Upper
BMI < 20 kg/m ²	0.710	2.033	0.588	7.036
BMI 20–24.9 kg/m ²	–1.465	0.231	0.085	0.627
BMI 25–29.9 kg/m ²	–0.332	0.718	0.326	1.582
BMI ≥ 30 kg/m ^{2c}	–	1	–	–
Age (years)	0.028	1.028	1.005	1.052
Gender (male)	1.315	3.724	1.464	9.473
Left ventricular ejection fraction (%)	–0.027	0.973	0.952	0.995
Systolic heart failure	–0.902	0.406	0.192	0.858
Ischemic cardiomyopathy	–0.226	0.798	0.398	1.600
Hypertension	0.519	1.680	0.784	3.600
Renal failure	0.301	1.351	0.640	2.855
Dyslipidemia	–0.508	0.602	0.321	1.127
ARBs ^d use	–1.011	0.364	0.182	0.728
Hemoglobin (g/dL)	–0.275	0.760	0.638	0.905
Handgrip strength (kg)	–0.066	0.936	0.891	0.985
Extracellular water ≥ 95th percentile	0.798	2.222	0.562	8.787
Cachexia ^e	–0.215	0.807	0.387	1.683

^a Beta coefficient.

^b Relative risk for the association with all-cause mortality.

^c Reference category.

^d Angiotensin II receptor blockers.

^e Subjects with an impedance vector on or outside of the lower pole of the 95% tolerance ellipse in the right side of the gender-specific RXc graph.

Table 3

Multivariate predictors of cardiovascular mortality in the study population (Cox proportional hazard regression analysis).

	<i>B</i> ^a	RR ^b	95% CI for RR	
			Lower	Upper
BMI < 20 kg/m ²	0.743	2.102	0.365	12.106
BMI 20–24.9 kg/m ²	–2.281	0.102	0.021	0.498
BMI 25–29.9 kg/m ²	–0.225	0.799	0.278	2.297
BMI ≥ 30 kg/m ^{2c}	–	1	–	–
Age (years)	0.044	1.045	1.009	1.081
Gender (male)	1.374	3.950	1.067	14.627
Left ventricular ejection fraction (%)	–0.032	0.969	0.939	0.999
Systolic heart failure	–1.263	0.283	0.094	0.848
Ischemic cardiomyopathy	–0.461	0.631	0.239	1.664
Hypertension	0.318	1.374	0.490	3.854
Renal failure	0.276	1.318	0.461	3.772
Dyslipidemia	–0.747	0.474	0.196	1.148
ARBs ^d use	–1.357	0.258	0.096	0.687
Hemoglobin (g/dL)	–0.354	0.702	0.542	0.909
Handgrip strength (kg)	–0.073	0.929	0.865	0.998
Extracellular water ≥ 95th percentile	0.832	2.299	0.224	23.627
Cachexia ^e	–0.498	0.608	0.211	1.755

^a Beta coefficient.

^b Relative risk for the association with cardiovascular mortality.

^c Reference category.

^d Angiotensin II receptor blockers.

^e Subjects with an impedance vector on or outside of the lower pole of the 95% tolerance ellipse in the right side of the gender-specific RXc graph.

systolic HF, as well as less mean handgrip strength, hemoglobin level, and LVEF. Use of ARBs was also lower in these patients.

Unadjusted survival after 3 years of follow-up was worse for underweight category than the others. However, after adjusting for all body composition, nutritional and clinical parameters differing at baseline, underweight patients were not at higher risk of all-cause and cardiovascular death compared with those with obesity, contrary to the previously found for other research groups, which have reported an inverse association between obesity and mortality in CHF patients.^{3,4}

Oreopoulos et al,²² in a recent meta-analysis of 9 observational HF studies demonstrated that compared with individuals without elevated BMI, and controlling for age, gender, and NYHA class, overweight (BMI 25–29.9 kg/m²) and obese (BMI ≥ 30 kg/m²) patients had a significantly lower cardiovascular and all-cause mortality risk at 2.7 y of follow-up. Moreover, prognosis was more favorable in obese patients compared with those who were overweight, supporting the hypothesis of the “obesity paradox”. Cicoira et al,²³ in one of the largest studies conducted to assess the prognostic value of BMI involved 5010 individuals, reported that the effect of BMI on prognosis is not related to more severe clinical conditions of patients with low BMI (<22 kg/m²), as it was independent of other strong prognostic markers like NYHA class, brain natriuretic peptide, inflammatory status and left ventricular function, and they suggested that BMI holds prognostic relevance per se. However, even when in this study results were controlled for some relevant variables, obesity was defined by an inaccurate method like BMI, which does not necessary reflect body fatness, neither fluid retention, but rather seems to be slightly more correlated with lean body mass than with percent body fat determined by direct measures.⁶ In addition, variables considered in the Cox regression model were categorized according to their median value, and not for a clinical cut-off; also, the inflammatory marker used was C-Reactive Protein, that is unspecific for the evaluation of inflammatory status in HF, and that have been found to be directly and independently associated with body fat.⁶

On 2003, Lavie et al²⁴ were the first in addressing the limitation of the lack of a detailed body composition evaluation by examining

the prognostic value of percent body fat, via the skinfold method, on 209 patients with chronic systolic HF (NYHA class I to III), and it was found that his results followed the same trend than the others previously reported at that moment. For every 1% absolute reduction in percent body fat, clinical events increased by >13%. However, these results were not adjusted for lean body mass; moreover, it is important to mention that skinfold method is not the best technique to estimate lean body mass in HF patients, since it could be confounded by fluid retention, which was not measured in that study.

In the present study, BMI was also used to define obesity in order to make the results more comparable with the most of the previously reported; however, indicators of depletion muscle mass and fluid retention were included in the model, as well as other prognostic markers that recently have been found to be important in the association between BMI and mortality, like HF etiology²⁵ and left ventricular systolic function.²⁶ After adjusting the Cox regression model, results suggested that being underweight, compared to being obese, was not an indicator of poor prognosis, independently of age, gender, LVEF, systolic HF, ischemic etiology, hypertension, renal failure, dyslipidemia, ARBs use, hemoglobin levels, handgrip strength, fluid retention (extracellular water ≥ 95 th percentile), and cachectic status. Moreover, normal weight patients seemed to enjoy a more favorable prognosis compared with those who were obese.

It is important to emphasize that in addition to age, gender, LVEF, systolic HF, and ARBs use, malnutrition markers like hemoglobin levels and handgrip strength were independent predictors for all-cause and cardiovascular mortality in this study, agree with the reported by other authors.^{10,27} Horwich et al.¹⁰ suggest that the poor prognosis of anemia in HF stems from malnutrition due to a catabolic state seen in advanced HF that is related to the neuro-hormone and immune disorders and associated with increases HF mortality. Meanwhile, Izawa et al.,²⁷ in a study in Japanese male with CHF, reported that handgrip strength was found to be a predictor of mortality in these patients; independently of LVEF and peak ventilatory oxygen uptake (VO_2). They hypothesized that this association could be due to the alterations in skeletal muscle ultrastructure and biochemical that occurred in patients with CHF, and when disease severity increase is muscle strength also affected. So that, it seems that muscle mass is an important indicator to be taking account in the prognosis evaluation of patients with CHF. These results also agree with those reported by Oreopoulos et al.,⁶ who gave lean mass (assessed by dual-energy X-ray absorptiometry) some relevance in the apparent obesity paradox.

Since the first reports of the obesity paradox in HF^{28,29}, several explanations have emerged. It have been postulated that because advanced HF is a catabolic state, patients progressing to higher levels of HF disease severity while carrying excess bodyweight have a greater metabolic reserve and are more resistant to the increasing catabolic burden. Also, adipose tissue has been shown to produce TNF- α receptors that could be protective. Additionally, it is possible that high circulating lipoprotein levels in obese patients may bind and detoxify lipopolysaccharides that play a role in stimulating the release of inflammatory cytokines, and it has found that overweight and obese patients with HF have lower levels of brain natriuretic peptide (BNP), all of which may serve to protect the obese patients with HF.^{3,4} However, regarding BNP, even when overweight and obese patients with HF have overlaid fluids, the intravascular compartment is usually underfilled,³⁰ and it could be the cause of lower levels of BNP, which does not necessarily reflects better conditions.

Even when all of this explanations could represent a valid paradoxical association between obesity and mortality, in light of our results, it seems that poor prognosis in underweight patients

with HF is related to a malnutrition status associated to an inflammatory responses, that Kalantar-Zadeh et al.⁵ have called “malnutrition-inflammation complex syndrome”.

An interesting finding was the lower use of ARBs in underweight patients, and we can hypothesize that in obese patients the higher utilization of ARBs could be related to better prognosis, as it was found to be an independent predictor of mortality, similar to the observed by other groups.³¹

In our study, it was not possible to assess inflammation, but underweight patient showed a poorer clinical and nutritional condition; moreover, among the independent predictive factors for all-cause and cardiovascular mortality in this study population were LVEF, handgrip strength and hemoglobin, all of them usually observed in over expressed inflammatory conditions.

5. Conclusion

A lower BMI does not predict all-cause and cardiovascular mortality among CHF patients independently of other nutritional, body composition, and clinical status parameters. In addition, in CHF patients more attention should be focused to optimize pharmacological treatment and the search of the underlying causes of underweight in order to give a more successful treatment and improve prognosis.

At present, it seems that in HF patients, being obese or increased their body weight should not be encourage, due this study showed a better prognosis for normal weight patients rather than for those obese.

6. Study limitations

The present study has four relevant limitations. First, the BMI value to define underweight was not that established for the World Health Organization ($\text{BMI} < 18.5$) due to there were few patients meeting this criteria; so we decided to modify the value from $<18.5 \text{ kg/m}^2$ to $<20 \text{ kg/m}^2$; second, indicators of an inflammatory status were not assessed; third, other malnutrition markers like serum albumin and total cholesterol were not available for all patients, so they were not analyzed; and fourth, the number of events per predictor included in the Cox regression analysis could have been insufficient and a type II error could have occurred in the estimates.

Conflicts of interest

All authors state no conflict of interest.

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