

Malnutrition in Outpatients with Heart Failure: Prevalence, Associated Factors and 6-Month Impact

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Abstract

Background: Malnutrition is common in heart failure with reduced ejection fraction (HFrEF) and may negatively affect prognosis.

Objective: To determine the prevalence of malnutrition in outpatients with HFrEF, identify associated clinical factors, and evaluate its impact on mortality and clinical outcomes at 6 months.

Methods: Prospective observational cohort study including 118 outpatients with HFrEF. Nutritional status was assessed using the Mini Nutritional Assessment (MNA) and the Subjective Global Assessment (SGA). Six-month follow-up documented mortality, hospitalizations, and emergency department visits.

Results: The prevalence of malnutrition was 21.2% (25/118). Malnourished patients were older (68 ± 12 vs. 60 ± 10 years; $p=0.001$), had a higher prevalence of NYHA functional class III–IV (45% vs. 15%; $p=0.002$) and atrial fibrillation (44% vs. 25%; $p=0.048$), and achieved a lower percentage of target beta-blocker dose (57.9% vs. 79.8%; $p=0.002$). No statistically significant difference in 6-month mortality was observed between the groups, although it was numerically higher in the malnourished group (14% vs. 4%; $p=0.082$). No differences were observed in hospitalization rates ($p=0.94$) or emergency department visits ($p=0.97$).

Conclusion: Malnutrition is present in approximately one in five outpatients with HFrEF, more common in the elderly and those with atrial fibrillation and was associated with a trend towards higher mortality in 6 months.

Keywords: Malnutrition; Heart Failure; Nutritional Status; Nutrition Assessment.

Introduction

Heart failure (HF) is a highly prevalent disease worldwide, affecting approximately 23 million people, with a progressive incidence. The increase in life expectancy resulting from therapeutic advances in cardiovascular diseases tends to raise, in the medium term, hospitalization rates, morbidities, and costs related to the care of these patients, consolidating HF as a significant public health problem.^{1–5}

Currently, several clinical and experimental studies have focused on the pathophysiology and factors associated with the disease for therapeutic optimization.⁶ Malnutrition is one of these factors, present mainly in more advanced stages.⁷ Research shows that the chronic catabolic state associated

with HF contributes to lean mass loss and cardiac cachexia, relating to a worse prognosis.^{8,9} However, in current guidelines, nutritional management is still undervalued, and its approach as a therapeutic focus lacks standardization.^{10–12}

Outpatient nutritional assessment is challenging. The relationship between HF and BMI (Body Mass Index) was suggested more than 10 years ago, although it is not a linear relationship. Patients with very low BMI, as well as obese patients, have worse clinical outcomes.^{13,14} However, the isolated use of BMI is limited, given the frequent fluid retention in these patients. Some assessment tools have been proposed, such as malnutrition scores like CONUT (Controlling Nutritional Status) and PNI (Prognostic Nutritional Index), although no methodology is universally accepted.^{7,15,16} More comprehensive methods, such as the Mini Nutritional Assessment (MNA)¹⁷ and the Subjective Global Assessment (SGA)¹⁸ have shown a more robust prognostic correlation,¹⁶ especially when performed by a multidisciplinary team.

Although malnutrition is associated with worse outcomes in patients with HF, data in the literature are still scarce. Therefore, identifying the prevalence of malnutrition in outpatients with heart failure with reduced ejection fraction (HFrEF), the associated factors, and assessing its impact

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Central Illustration: Malnutrition in Outpatients with Heart Failure: Prevalence Associated Factors and 6-Month Impact

ABC Heart Failure & Cardiomyopathy

MALNUTRITION IN HF: PREVALENCE, ASSOCIATED FACTORS AND 6-MONTH IMPACT**Prevalence****21.2%**

Malnutrition in patients with HFrEF

Associated Factors**Advanced age** ($p=0.001$)
Worse NYHA functional class ($p=0.002$)
Atrial fibrillation ($p=0.048$)
Lower dose of beta-blocker ($p=0.002$)**Prognosis****MORTALITY**
3.5 times higher
($p=0.082$)

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on mortality and clinical outcomes at 6 months becomes essential.

The main findings in this study, including the prevalence of malnutrition, associated clinical factors, and its prognostic impact at 6 months, are summarized in the central figure.

Methods

This study was approved by the Research Ethics Committee of the Pontifical Catholic University of Paraná, under opinion number 3.043.474, dated 11/28/2018. All participants signed the Informed Consent Form before their inclusion. The study was conducted in accordance with the provisions of Resolution 466/2012 of the National Health Council.

Study population

This is a prospective, single-center, observational cohort study of HF patients followed up as outpatients for 6 months.

Eligible participants for the study were: patients over 18 years of age, of both sexes, undergoing outpatient follow-up for HF, with an ejection fraction of less than 50%, who had not been hospitalized in the previous 30 days, and who signed the informed consent form.

Patients with HF (ejection fraction $\leq 50\%$) were consecutively included, aged ≥ 18 years, in outpatient follow-up referred to the HF outpatient clinic of a tertiary hospital in Curitiba, PR. Sample obtained by convenience, including participants who were available and accessible at the time of data collection. Exclusion criteria: inability to obtain follow-up data. Demographic data and associated medical history, such as comorbidities and ongoing medications, were collected. The flowchart of the study sample selection is illustrated in Figure 5.

Data collection

The patients were included according to scheduling at the specialized outpatient clinic of a tertiary hospital in Curitiba, PR, based on the inclusion criteria. Patient information was collected from a patient identification form (Appendix 1) administered by the researchers at the time of consultation, which included information necessary for the study: age, sex, weight, height, medications in use and dosage of medications prescribed for HF, demographic characteristics, comorbidities, etiology of HF, ejection fraction, and data from the physical examination performed during the consultation.

In parallel with the selection of patients for the study by the medical team, a nutritional assessment was carried out, based on the application of the Mini Nutritional Assessment (MNA) full version^{19,17} and the Subjective Global Assessment (SGA)^{18,20} (appendix 2), which are essential in the nutritional classification of these patients. The MNA classifies the patient into normal nutritional status (24-30 points), at risk of malnutrition (17-23.5 points), and malnourished (<17 points), while the SGA classifies: A (well-nourished), B (moderately malnourished), and C (severely malnourished). The instruments were applied consecutively, during the same assessment by a trained nutritionist.

Six months after the initial assessment, patient records were reviewed for information on hospitalizations, emergency room visits due to disease decompensation, and mortality. In those cases where the necessary information was missing from the records, when feasible, telephone contact was made with a previously registered number. Despite being an extremely important factor in daily clinical practice, due to logistical limitations of the study, nutritional follow-up by a nutritionist was not carried out in this work.

Outcomes and follow-up

Follow-up of all patients was conducted via telephone contact (with the patient or family members) and review of medical records, 6 months after the date of the initial in-person assessment, based on a new questionnaire about outcomes: mortality, hospitalizations, and seeking emergency care.

The primary outcome is the assessment of the prevalence of malnutrition in patients with HF through evaluation by a nutritionist. Secondary outcomes include evaluating the existence of factors related to malnutrition and analyzing the impact of malnutrition in relation to hospitalizations and emergency room visits at any healthcare facility, and mortality within 6 months.

Statistical analysis

The data were obtained by the researcher and recorded on the data collection instrument. This data will be entered into a spreadsheet (Microsoft Excel®), checked, and exported for subsequent statistical analysis.

Statistical analyses were performed using Stata 11 software. Continuous variables were described as mean $\pm$ standard deviation and compared between groups (malnourished vs. non-malnourished) using Student's t-test for independent samples. Categorical variables were described as frequencies and percentages and compared using appropriate association tests. The association between quantitative variables was assessed using Pearson's correlation coefficient.

To assess factors associated with malnutrition, exploratory multivariate logistic regression was performed, including clinically relevant variables (age, functional class, and percentage of the target dose of beta-blockers). A statistical significance level of $p < 0.05$ (two-tailed) was adopted. Data were analyzed using Stata 11.

Results

One hundred and eighteen consecutive patients were included, from January to September 2019, in outpatient follow-up for HF, the majority were men (67.8%), with a mean age of 61 ± 11 years. The mean ejection fraction was 32%, and most patients were in functional class I or II. The main characteristics of the studied population are shown in Table 1.

The prevalence of malnutrition in this population, according to the nutritionist's assessment, was 21.2% of cases, as illustrated in the central figure, including sarcopenic obese individuals. The classification of each patient according to this assessment is shown in Figure 1.

In the comparison between the two groups, malnourished patients were older (67.8 ± 12 vs. 59.29 ± 10 , $p = 0.001$) and had more advanced FC ($p = 0.002$ - figure 2). In addition, there was a higher prevalence of atrial fibrillation in malnourished patients compared to non-malnourished patients (44% vs. 25%, with $p = 0.048$).

Furthermore, the tolerated dose of beta-blockers was lower in malnourished individuals (79% of the target dose in non-malnourished individuals vs. 57.9% in malnourished

individuals, $p = 0.002$) (Figure 3). There was no difference in comorbidities between the groups, nor was there any influence from disease duration, number of previous hospitalizations, or percentage of the target dose of other medications.

The percentage of the target dose of medications indicated for the treatment of HF and the average dose of diuretic used (in our sample, represented by furosemide) are shown in Table 2. In an exploratory multivariate analysis, age, functional class, and percentage of the target dose of beta-blockers were associated with malnutrition. The other parameters did not show a statistically significant association.

The mortality rate varied between the groups, with a greater statistical tendency in the malnourished group (14% of malnourished vs. 4% of non-malnourished, $p = 0.082$ - Figure 4). There was no difference between the groups regarding hospitalizations or seeking emergency care (Table 3).

Discussion

In this prospective observational cohort study, we evaluated the association of malnutrition in outpatients with HFrEF with clinical parameters and outcomes during a six-month follow-up. Although the study has a prospective cohort design, the prevalence of malnutrition was estimated from the cross-sectional assessment performed at the time of patient inclusion. Ideally, this diagnosis should be made in a multidisciplinary and multiparametric manner, with DEXA (Dual-Energy X-ray Absorptiometry) assessment being the gold standard for diagnosing sarcopenia, based on the measurement of percentage of fat, lean mass, and bone mass.²¹ However, this methodology is still not widely available, especially in the context of the Brazilian Unified Health System (SUS).

In studies that used parameters similar to the present work, the prevalence was around 17% to 25%,^{22,23} consistent with our finding of 21.2%. Considering that this means that about one in five patients with HF presents some degree of malnutrition, recognizing this problem and the factors related to it becomes extremely relevant.

In this sense, it is important to know the population most susceptible to malnutrition among patients with HF. Recent studies show that these are men,^{24,25} of advanced age,²³⁻²⁵ with poorer functional class and a higher prevalence of atrial fibrillation,^{24,25} as confirmed in our findings. Furthermore, they also demonstrate that these patients present more renal dysfunction, anemia, and altered mobility, which were not evaluated in our study. By identifying the subgroup at highest risk of malnutrition, it is possible to optimize non-pharmacological treatment with nutritional guidance.

Another relevant finding was that malnourished patients tolerate lower doses of beta-blockers. Several studies link lower beta-blocker dosages to a higher incidence of cardiac cachexia and weight loss.^{26,27} However, cachexia and malnutrition, although closely related, differ substantially from each other.²⁶ While malnutrition in HF results from

Table 1 – Baseline characteristics of the study population by nutritional status

	Total (n=118)	Not malnourished (n=93)	Malnourished (n=25)	p-value
Demographics				
Age (years)	61±11	59.29±10	67.83±12	0.001
Sex (male), n (%)	80 (67.8)	64 (69)	16 (64)	0.65
Smoking, n (%)	48 (40.7)	41 (44)	7 (28)	0.15
Alcoholism, n (%)	18 (15.3)	15 (16)	3 (12)	0.61
Ejection fraction (average)	32±8	32±8	32±8	0.77
FC, n (%)				0.002
I	43 (37.4)	39 (43)	4 (17)	
II	47 (40.9)	38 (42)	9 (38)	
III	21 (18.3)	13 (14)	8 (33)	
IV	4 (3.5)	1 (1)	3 (12)	
Etiology of HF, n (%)				0.92
Ischemic	50 (42.3)	37 (40)	13 (52)	
Idiopathic	19 (16.1)	16 (17)	3 (12)	
Chagas disease	13 (11)	12 (13)	1 (4)	
Valvar	8 (6.8)	5 (5)	3 (12)	
Hypertensive	3 (2.5)	2 (2)	1 (4)	
Others	25 (21.3)	21 (23)	4 (16)	
Duration of illness, in years (median)	8 (3, 14)	9 (1, 30)	9 (1, 12)	
Number of previous hospitalizations (average)	3.01	2±4	3±3	0.49
Comorbidities				
Diabetes, n (%)	45 (38.1)	36 (39)	9 (36)	0.88
HBP, n (%)	86 (72.9)	69 (74)	17 (68)	0.54
DSLIP, n (%)	55 (46.6)	42 (45)	13 (52)	0.54
PAOD, n (%)	12 (10.3)	9 (18)	3 (12)	0.78
Thyroid disease, n (%)	32 (27.1)	25 (27)	7 (28)	0.91
Atrial fibrillation, n (%)	33 (28.2)	22 (24)	11 (44)	0.048
Medications				
ACEI, n (%)	43 (36.4)	35 (37.6)	8 (32)	
ARB, n (%)	27 (22.9)	22 (23.7)	5 (20)	
Sacubitril/valsartan, n (%)	38 (32.2)	29 (31.2)	9 (36)	
Beta-blocker, n (%)	115 (97.5)	90 (96.8)	25 (100)	
Spironolactone, n (%)	91 (77.1)	71 (76.3)	20 (80)	
Diuretic, n (%)	92 (78)	69 (74.2)	22 (88)	
Digoxin, n (%)	28 (23.7)	21 (22.6)	7 (28)	
Vasodilator, n (%)	29 (24.6)	24 (25.8)	5 (20)	
Statin, n (%)	83 (70.3)	65 (69.9)	18 (72)	
ASA, n (%)	62 (52.5)	49 (52.7)	13 (52)	

FC: functional class; HF: heart failure; HBP: hypertension; DSLIP: dyslipidemia; PAOD: peripheral arterial occlusive disease; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ASA: aspirin.

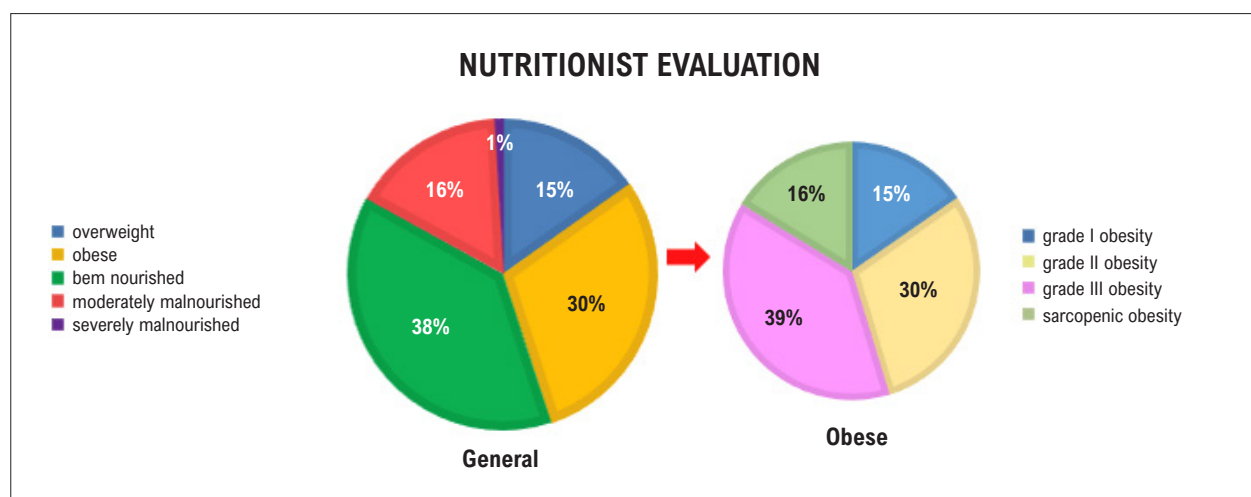


Figure 1 – Classification of patients according to subgroups by the nutritionist.

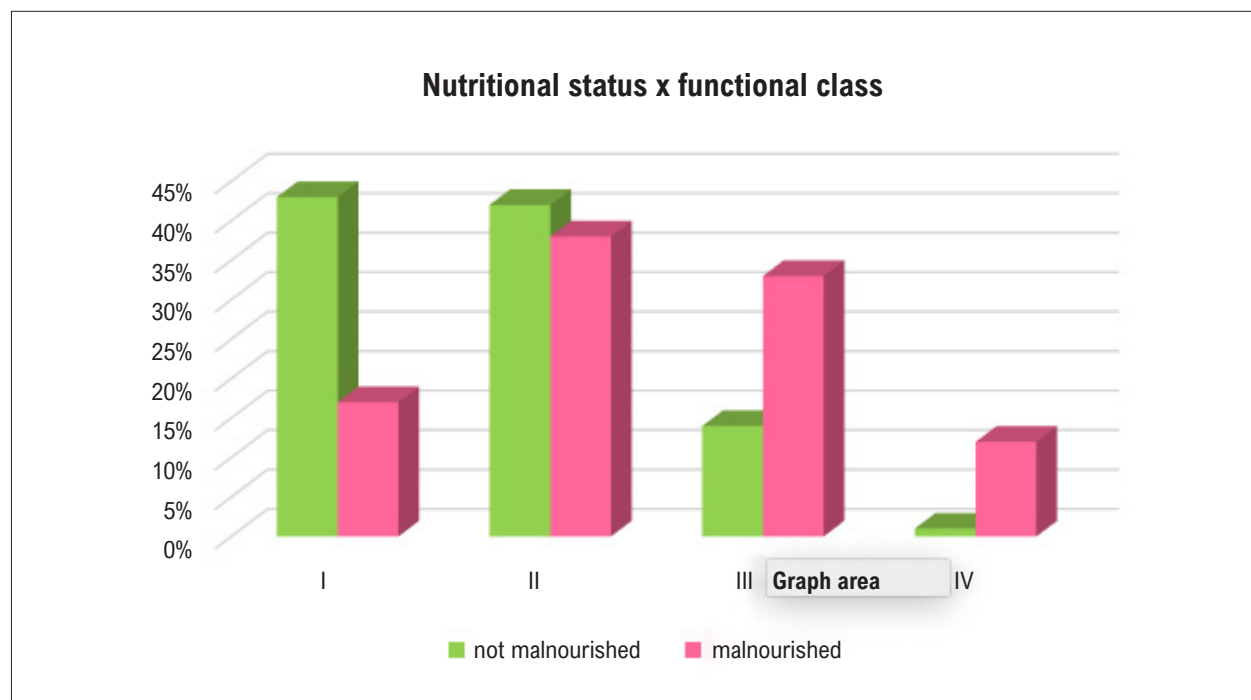


Figure 2 – Comparison between functional class and nutritional status of the patient.

malabsorption secondary to edema of the gastrointestinal tract wall and limitations in eating and food preparation due to fatigue and dyspnea,²⁶ cachexia is related to the inflammatory process common to chronic diseases, which activates various hormonal cascades, especially sympathetic activation.²⁷ This activation causes increased energy consumption, myotoxicity, and increased insulin resistance, resulting in muscle cell loss and weight loss, characterizing cardiac cachexia.²⁷ Since cachexia is related to sympathetic system activation, it is expected that beta-blockers will have a beneficial effect in its prevention, and

some studies have already shown this benefit.^{26,27} However, data correlating malnutrition with reduced tolerance to beta-blockers are scarce, and our work is one of the few to document this correlation.

Regarding patient follow-up, our data showed a trend toward higher mortality among malnourished individuals, as already presented in other studies in the literature,^{7,9,14,15,23,25} malnutrition may represent a prognostic risk factor in HF. Although exploratory multivariate analysis suggests an independent association between some clinical factors and malnutrition, these findings should be interpreted with

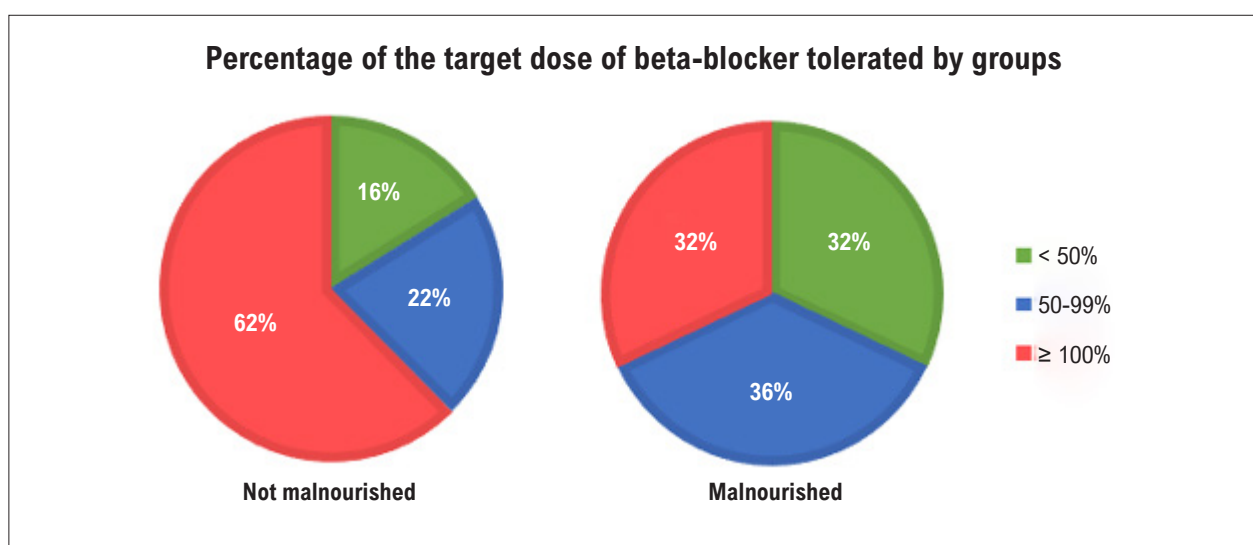


Figure 3 – Comparison between the percentage of the target dose of beta-blocker tolerated by each group, according to the patient's nutritional status.

Table 2 – Target dose of medications and average dose of diuretic by nutritional status group

Medications	Not malnourished	Malnourished	p-value
% target dose of beta-blockers	79.8	57.9	0.002
% target dose ACEI/ARB	72	71	0.91
% target dose Sacubitril/valsartan	66	61	0.63
% target dose of spironolactone	98	96	0.39
Diuretic dose (in mg)	69	22	0.14

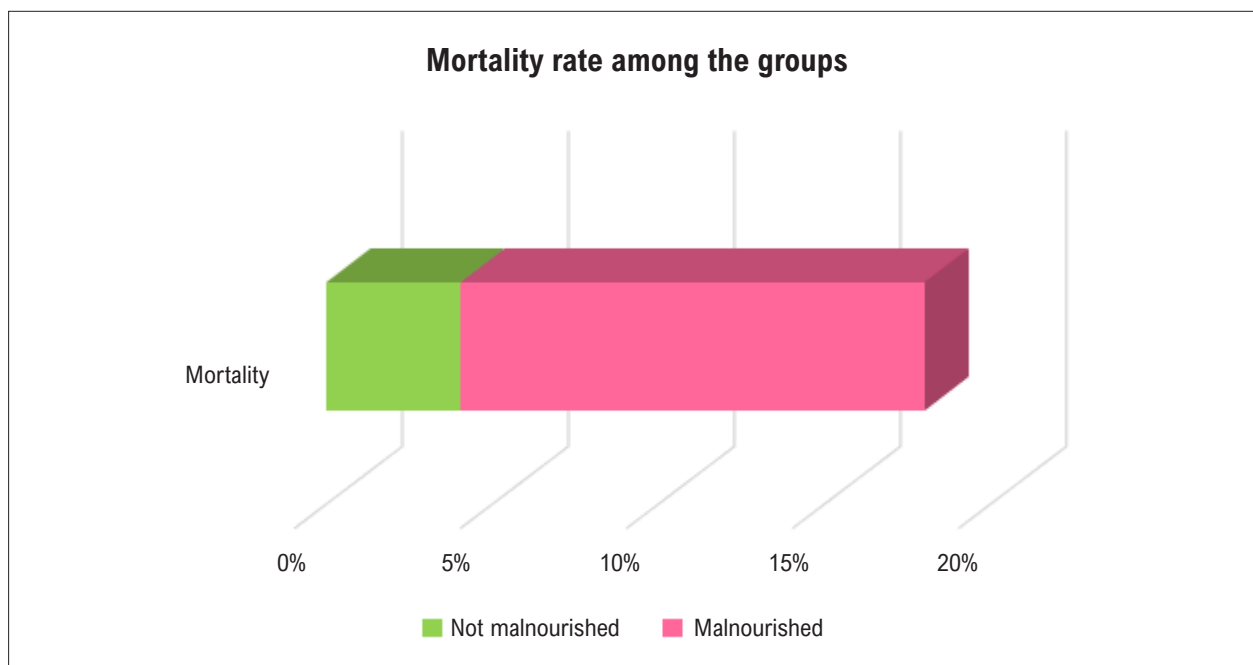


Figure 4 – Mortality rate among the groups, according to nutritional status.

Table 3 – Patient follow-up at 6 months – mortality rate, hospitalizations, and emergency room visits by group

Follow-up	Not malnourished	Malnourished	p-value
Mortality, n (%)	3 (4)	3 (14)	0.082
Hospitalizations, n (%)	15 (20)	4 (19)	0.94
Number of hospitalizations (average)	1	1.5	0.002
Emergency care demand	7 (9)	2 (10)	0.97
Number of demands (average)	1.6	1.5	0.91

caution, considering the sample size and the significant loss to follow-up due to failure to communicate with study patients via previously established communication channels.

There is a high prevalence of malnutrition in patients with HFrEF, and this study highlights a possible association with worse clinical outcomes. Identifying the correct nutritional status can be challenging, and proper nutritional screening involving a multidisciplinary team becomes essential.

In summary, the Central Figure integrates the relationship between the prevalence of malnutrition, associated clinical factors, and the observed prognostic impact.

Limitations of the study

The study conducted had significant limitations. This is a prospective observational cohort study in which nutritional assessment was performed at baseline, and patients were followed for 6 months to evaluate clinical outcomes. This design allows for the assessment of associations and the exploration of the prognostic impact of malnutrition, although it does not allow for establishing causality. The population defined for this study was limited to a single center and included a small sample of patients (n=118), a limiting factor for extending its results to other regions. Furthermore, during data collection, potential confounding factors such as dietary control, therapeutic adherence, or physical activity, which directly influence the nutritional status of patients, were not mentioned.

It is also worth noting that patients in outpatient follow-up tend to have greater medication adherence when compared to the general population, which could be a selection bias.

Regarding follow-up, the short period of only 6 months is insufficient to identify potential outcomes in the monitoring of these patients. Furthermore, there was a sample loss of 18% of the patients initially included in the study, a limiting factor for drawing more conclusive prognostic conclusions. This is due either to the lack of a follow-up appointment within 6 months or to difficulties in contacting them by telephone.

Finally, the multivariate analysis was exploratory in nature and was not subjected to formal model validation or calibration analysis, which limits causal inferences and the robustness of the adjusted estimates.

Conclusion

The prevalence of malnutrition among patients with HF is high, despite being underdiagnosed. Therefore, identifying

the subgroup at highest risk, as well as the factors associated with this condition, becomes essential.

Factors such as advanced age, poorer functional class, and the presence of atrial fibrillation may be associated with a worse clinical outcome, including lower tolerance to standard therapy and, especially, a greater tendency towards 6-month mortality in malnourished patients.

Early diagnosis and proper management are essential for clinical optimization and prevention of adverse outcomes. Given the relevance of the topic, future studies that expand the population, their comorbidities, and nutritional status, as well as the follow-up of these patients, are extremely important.

Author Contributions

Conception and design of the research: Freitas AKE, Moura LAZ, Bonatto M, Marzagao V; Acquisition Contini A of data: Gondo LA, Marzagao V, Voigt G, Centenaro F, Konno C, Lemke A; Analysis and interpretation of the data: Gondo LA, Freitas AKE, Moura LAZ, Bonatto M, Marzagao V; Statistical analysis: Freitas AKE; Writing of the manuscript: Gondo LA, Freitas AKE, Voigt G, Centenaro F, Konno C, Lemke A, Contini A; Critical revision of the manuscript for intellectual content: Gondo LA, Freitas AKE, Moura LAZ, Bonatto M.

Potential Conflict of Interest

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

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Pontifícia Universidade Católica do Paraná under the protocol number 3.043.474. 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.

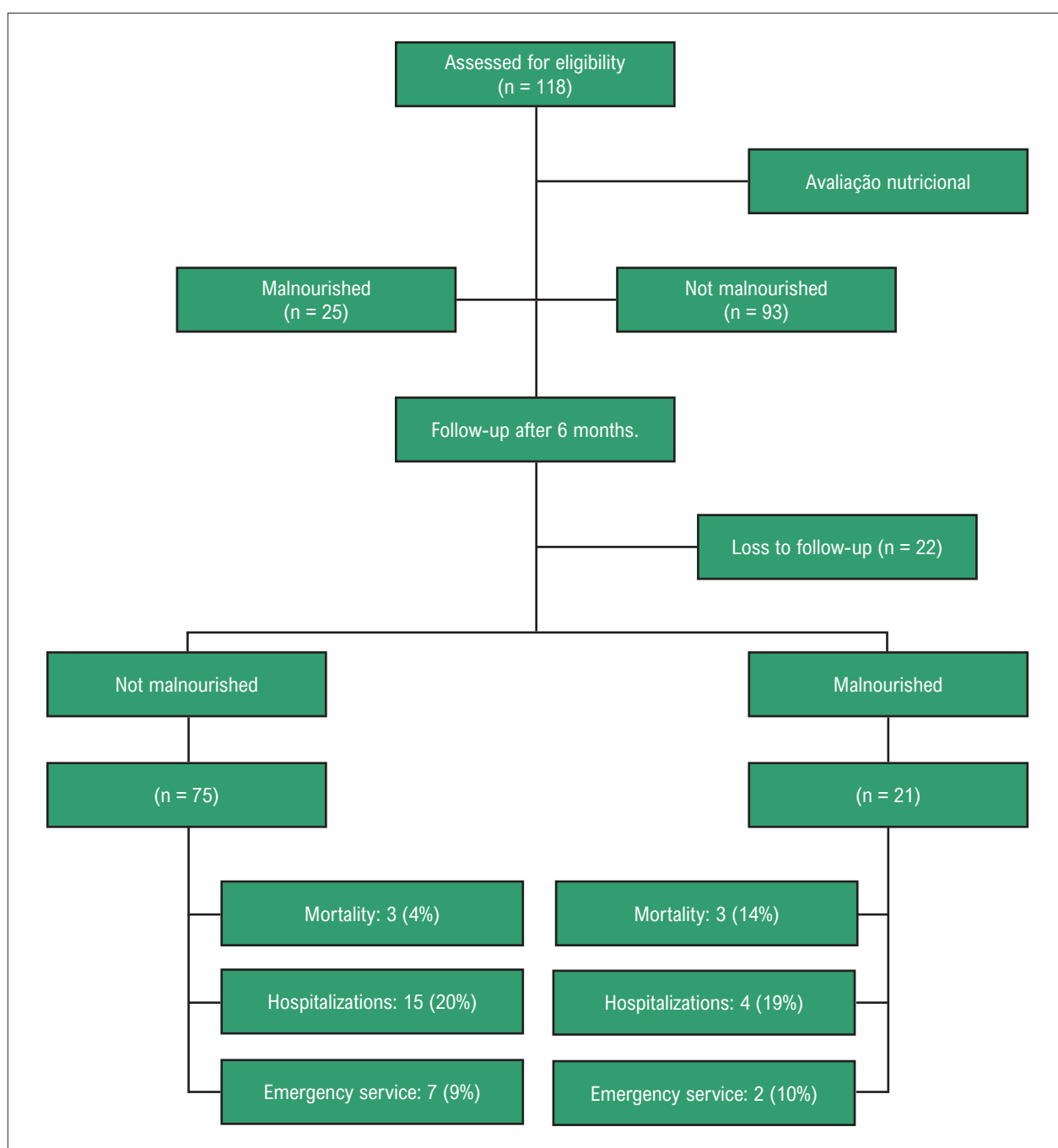


Figure 5 – Flowchart of the study sample selection.

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