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ORIGINAL ARTICLES

Relationship of overweight and obesity with adverse clinical outcomes in adult patients with heart failure in a Latin American hospital

Relação entre sobrepeso e obesidade com desfechos clínicos adversos em pacientes adultos com insuficiência cardíaca em um hospital latino-americano

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Abstract

Aim: This study aimed to determine the association between overweight, obesity and adverse clinical outcomes in adult patients diagnosed with heart failure in a Latin American hospital during 2023. **Methods:** A secondary cross-sectional study was conducted including patients aged ≥18 years with heart failure diagnosed by clinical, echocardiographic, and ICD-10 criteria. Body mass index was used to classify weight status. Logistic regression models estimated odds ratios with 95% confidence intervals. Machine learning models were applied to identify factors associated with adverse clinical outcomes. **Results:** Male sex was more prevalent among patients with adverse clinical outcomes (p=0.04). Pulmonary hypertension was significantly more frequent in underweight patients (p<0.001). Age ≥60 years (OR 5.64; 95% CI 2.27–14.83) was associated with higher odds of adverse outcomes, whereas overweight was associated with lower odds (OR 0.23; 95% CI 0.08–0.65). Random Forest analysis identified age as the most relevant variable. **Conclusions:** Overweight was associated with a lower probability of adverse clinical outcomes in hospitalized patients with heart failure, while older age was associated with worse outcomes. These findings should be interpreted with caution due to the composite outcome and potential residual confounding.

Keywords: Body mass index. Obesity. Overweight. Heart failure. Obesity paradox. Adverse clinical outcomes.

Resumo

Objetivo: Este estudo teve como objetivo determinar a associação entre sobrepeso, obesidade e desfechos clínicos adversos em pacientes adultos diagnosticados com insuficiência cardíaca em um hospital latino-americano durante o ano de 2023. **Métodos:** Foi realizado um estudo transversal secundário incluindo pacientes com idade ≥18 anos com insuficiência cardíaca diagnosticada por critérios clínicos, ecocardiográficos e da CID-10. O índice de massa corporal foi utilizado para classificar o estado ponderal. Modelos de regressão logística estimaram as razões de chances (OR) com intervalos de confiança de 95%. Modelos de aprendizado de máquina foram aplicados para identificar fatores associados a desfechos clínicos adversos. **Resultados:** O sexo masculino foi mais prevalente entre os pacientes com desfechos clínicos adversos (p=0,04). A hipertensão pulmonar foi significativamente mais frequente em pacientes com baixo peso (p<0,001). A idade ≥60 anos (OR 5,64; IC 95% 2,27–14,83) foi associada a maiores chances de desfechos adversos, enquanto o sobrepeso foi associado a menores chances (OR 0,23; IC 95% 0,08–0,65). A análise de Random Forest identificou a idade como a variável mais relevante. **Conclusões:** O sobrepeso foi associado a uma menor probabilidade de desfechos clínicos adversos em pacientes hospitalizados com insuficiência cardíaca, enquanto a idade avançada foi associada a piores desfechos. Esses achados devem ser interpretados com cautela devido ao desfecho composto e ao potencial de fatores de confusão residuais.

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Palavras-chave: Índice de massa corporal. Obesidade. Sobrepeso. Insuficiência cardíaca. Paradoxo da obesidade. Desfechos clínicos adversos.

Introduction

Overweight and obesity are characterized by excessive accumulation of body fat, with obesity being recognized as a chronic, multifactorial disease associated with adverse health outcomes. According to the World Health Organization, in 2022, 43% of adults were overweight and 16% were obese (1). In the Americas, the prevalence reaches 67.5% for overweight and 33.8% for obesity (2). In Colombia, 37.7% of adults are overweight and 18.7% are obese (3).

Overweight and obesity are strongly associated with chronic noncommunicable diseases, including heart failure. Globally, approximately 56.5 million people were living with heart failure in 2021 (4). In Colombia, the estimated prevalence exceeds one million individuals (5).

In this context, several studies have evidenced a phenomenon known as the obesity paradox, which suggests that obesity may be associated with better clinical outcomes in patients with heart failure (6). One of the first studies to describe the relationship was conducted in the United States (USA) by Horwich et al., who, after a five year follow up of 1.203 patients with heart failure, observed that those classified as overweight or obese according to their BMI had a longer clinical survival compared to those with normal weight or underweight (7). Similar findings have been reported in large European cohorts (8).

Several mechanisms have been proposed, including greater metabolic reserve, protective effects of adipokines, and differences in inflammatory profiles. However, alternative explanations such as reverse causation, sarcopenia, and limitations of body mass index as a surrogate of body composition have also been suggested. In this line, Sharma et al. found that patients with chronic HF and low weight had an increased risk of adverse clinical outcomes, including cardiovascular events and hospitalizations, whereas these risks were significantly lower in overweight or obese individuals (9).

Given that most evidence originates from high-income countries, there is a need to generate data in Latin American populations. Therefore, this study aimed to evaluate the association between overweight, obesity, and adverse clinical outcomes in hospitalized patients with heart failure in a Latin American hospital during the year 2023.

Material and Methods

A secondary cross-sectional study was conducted targeting adult patients (≥18 years) with a diagnosis of heart failure hospitalized at Hospital Universidad del Norte, Soledad, Colombia, during 2023. The accessible population included those patients with a diagnosis of heart failure, identified by clinical history, clinical criteria, echocardiographic findings and/or diagnostic coding according to the ICD-10, who were hospitalized between February and July 2023 in the emergency department, general ward or intensive care unit and who had complete information in the institutional database, including sociodemographic, clinical and anthropometric variables. The body weight of all patients was obtained at the time of hospital admission. Inclusion criteria were: age 18 years or older and hospital stay of more than 24 hours during the study period.

Body mass index calculated as weight in kilograms divided by height in meters squared (kg/m^2), was used to classify the body weight of the patients. This measure, recommended by the WHO, allows categorization of body weight into the following categories: underweight (BMI <18.5), normal weight (BMI between 18.5 and 24.9), overweight (BMI between 25.0 and 29.9) and obese (BMI ≥30.0) (10). BMI is a widely used tool in clinical research because it is simple, non-invasive- low cost and useful for assessing the risk associated with clinical outcomes in different population contexts (1).

Adverse clinical outcomes were defined as the occurrence of clinically relevant events during hospitalization, including acute coronary syndrome, cardiogenic shock, arrhythmias, acute pulmonary edema, and pulmonary hypertension.

A composite outcome was used to capture the overall burden of complications during hospitalization. However, given the heterogeneity of these events in terms of pathophysiology and prognostic significance, individual outcomes were also analyzed descriptively.

Sociodemographic variables such as age and sex were included, as well as relevant clinical variables, including serum levels of total cholesterol (TC), low density lipoprotein (LDL), triglycerides (TG) and history of smoking. Additionally, anthropometric variables were considered, specifically BMI, calculated from recorded weight and height.

Categorical variables were expressed as absolute frequencies and percentages. To compare differences between subgroups defined by BMI categories, the chi-square test or Fisher's exact test was used for categorical variables. Variables associated with adverse clinical outcomes were initially explored using a Random Forest classification model. The model was implemented using a supervised learning approach, and variable importance was assessed using the decrease in F1-score. Due to the sample size, internal validation was performed without a separate external validation dataset. The Random Forest model was used as an exploratory tool to identify relevant variables for inclusion in the multivariate regression model. The discriminative performance of the model was assessed by the area under the ROC curve, and the model fit was verified by the Hosmer-Lemeshow test. Values of $p < 0.05$ were considered statistically significant. Data processing and analysis was performed using R software version 4.4.0.

This study was carried out in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki for research on human subjects. The research was approved by the Research Ethics and Committee of the Universidad del Norte (record No. 287, March 30, 2023). According to the Resolution 8430 de 1993 of the Colombian Ministry of Health, in its Article 11, which establishes the scientific, technical and administrative norms for health research, this study is classified as a research without risk.

Results

A total of 215 patients were initially identified; 34 were excluded due to pulmonary thromboembolism, chronic liver disease, or acute kidney injury, resulting in a final sample of 181 patients. Baseline sociodemographic and clinical characteristics according to BMI categories are presented in **Table 1**. No statistically significant differences were observed across BMI groups for the evaluated variables.

The distribution of adverse clinical outcomes according to BMI categories is shown in **Table 2**. Pulmonary hypertension was significantly more frequent in underweight patients, whereas no statistically significant differences were observed for the remaining outcomes.

Table 3 summarizes patient characteristics according to the presence of adverse clinical outcomes. Male sex was more frequent among patients with adverse outcomes, while no statistically significant differences were observed for the remaining variables.

Multivariate analysis results are presented in **Table 4**, where age ≥60 years was associated with higher odds of adverse clinical outcomes, whereas overweight was associated with lower odds.

The Random Forest analysis (**Figure 1**) identified age and BMI as the most relevant variables, followed by LDL, smoking, chronic kidney disease, and triglycerides.

TABLE 1 - Characteristics of patients with heart failure in a Latin American hospital (n=181), according to bmi.

Variable, n (%)	Underweight (<18 kg/ m^2) n=16	Normal weight (18.5–24.9) n=96	Overweight (25–29.9) n=38	Obese (≥30) n=31	p-value*
Male	8 (50.0)	52 (54.2)	21 (55.3)	13 (41.9)	0.65
Age >60	14 (87.5)	79 (82.3)	29 (76.3)	24 (77.4)	0.74
Smoking	9 (56.3)	39 (40.6)	13 (34.2)	11 (35.5)	0.47
High TC	1 (6.7)	13 (18.1)	5 (17.2)	6 (31.6)	0.34
High LDL	5 (35.7)	33 (48.5)	15 (51.7)	11 (57.9)	0.64
High TG	1 (7.1)	6 (8.6)	3 (10.3)	4 (21.1)	0.50
Arterial hypertension	12 (75.0)	79 (82.3)	33 (86.8)	27 (87.1)	0.68
Type 2 diabetes	5 (31.3)	35 (36.5)	14 (36.8)	13 (41.9)	0.91
CKD	9 (56.3)	48 (50.0)	15 (39.5)	8 (25.8)	0.08

LDL, low density lipoprotein; CKD, chronic kidney disease; TC, total cholesterol; TG, triglycerides;
The number of observations varied across variables due to missing data, including TC (n=135), LDL cholesterol (n=130), and TG (n=132). Percentages were calculated based on available data for each variable. *Chi-square test.

TABLE 2 - Clinical and biochemical characteristics of patients according to adverse clinical outcome.

Variable, n (%)	Yes n=152	No n=29	p-value*
Male	84 (55.3)	10 (34.5)	0.04
Age >60	126 (82.9)	20 (69.0)	0.12
Smoking	65 (42.8)	7 (24.1)	0.07
High TC	21 (84.0)	4 (16.0)	0.15
High LDL	54 (84.4)	10 (15.6)	0.30
High TG	11 (78.6)	3 (21.4)	0.14
Arterial hypertension	126 (82.9)	25 (86.2)	0.79
Type 2 diabetes	54 (35.5)	13 (44.8)	0.40
CKD	68 (44.7)	12 (41.4)	0.84

LDL, low density lipoprotein; CKD, chronic kidney disease; TC, total cholesterol; TG, triglycerides.
The number of observations varied across variables due to missing data, including TC (n=135), LDL cholesterol (n=130), and TG (n=132). Percentages were calculated based on the available data for each variable. *Chi-square test

TABLE 3 - Acute complications in patients with heart failure in a Latin American hospital (January-June 2023) according to BMI category.

Variable, n (%)	Underweight n=16	Normal weight n=96	Overweight n=38	Obese n=31	p-value*
Acute coronary syndrome	7 (43.8)	51 (53.1)	11 (29.0)	11 (35.5)	0.05
Cardiogenic shock	2 (12.5)	10 (10.4)	1 (2.6)	2 (6.5)	0.44
Acute pulmonary edema	3 (18.8)	18 (18.8)	6 (15.8)	5 (16.1)	0.98
Pulmonary hypertension	9 (56.3)	21 (21.9)	4 (10.5)	2 (6.5)	<0.001
Arrhythmia	9 (56.3)	29 (30.2)	10 (26.3)	8 (25.8)	0.13

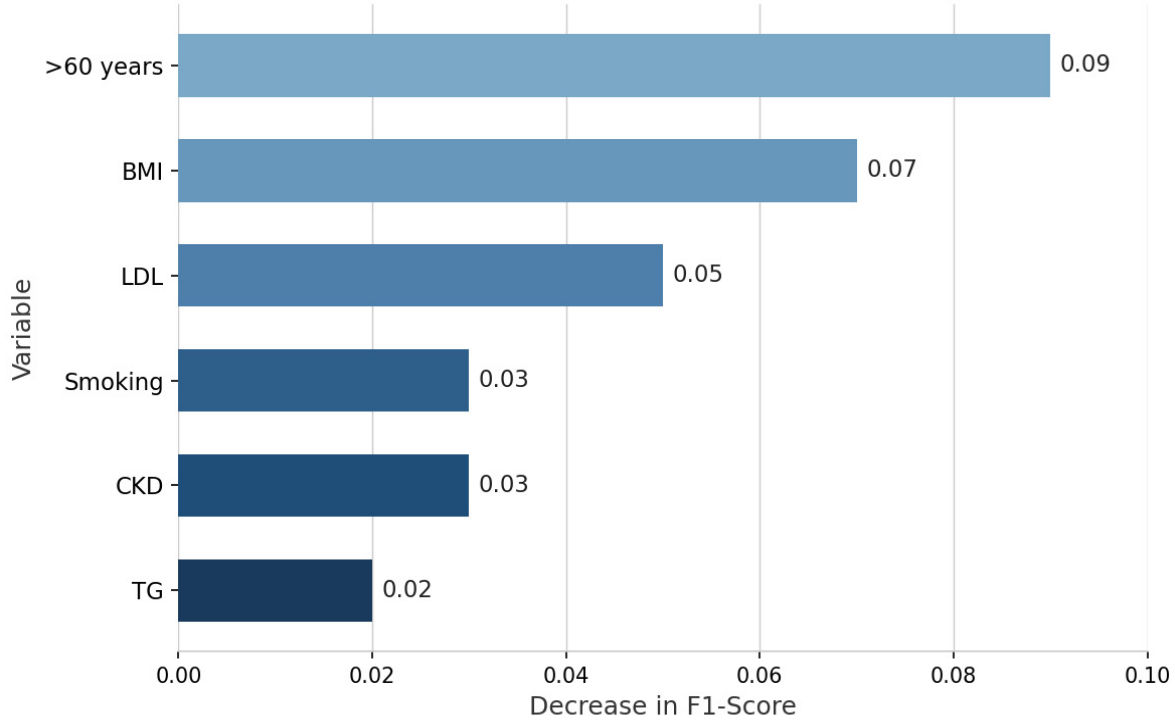
*Chi-square test.

TABLE 4 - Factors associated with complications in patients with heart failure in a Latin American hospital in the period January-June 2023.

Variable	Adjusted OR (95% IC)*	p-value
Age ≥ 60	5.64 (2.27 - 14.83)	< 0.001
BMI (Underweight)	0.42 (0.10 - 2.05)	0.28
BMI (Overweight)	0.23 (0.08 - 0.65)	0.004
BMI (Obese)	0.63 (0.17 - 2.42)	0.52
Female Sex	0.79 (0.32 – 1.92)	0.60
Smoking	2.31 (0.88 - 6.55)	0.09
TC	0.58 (0.18 – 1.87)	0.36
TG (High risk)	0.34 (0.10 – 1.16)	0.08
LDL (High risk)	0.57 (0.21 – 1.51)	0.26

BMI, body mass index; LDL, low density; TC, total cholesterol; TG, triglycerides.
*Firth penalized logistic regression model to reduce small-sample bias. Variables included in the model were selected based on clinical relevance and prior exploratory analyses. Model discrimination was assessed using the area under the receiver operating characteristic curve, and calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test.

Figure 1 - Decrease in F1-Score when eliminating each predictor variable in the Random Forest model for adverse clinical outcomes in a Latin American hospital in the period January-June 2023.



The bar indicates how much the F1-Score decrease when each covariate is excluded: Age (> 60 years), BMI, LDL (High risk), Smoking, CKD and TG (High risk). BMI, body mass index; LDL, low density lipoprotein; CKD, chronic kidney disease; TG, triglycerides.

Discussion

This study evaluated the association between BMI categories and adverse clinical outcomes in hospitalized patients with heart failure in a Latin American setting. We found that age older than 60 years was associated with worse clinical outcomes, whereas overweight was associated with lower odds of complications. The BMI categories with the highest significant frequency of pulmonary hypertension cases were underweight and normal weight.

Fei Xu, Chen Zhang et al. reported a higher frequency of clinical outcomes in patients with heart failure older than 60 years, a finding that agrees with the results of our study, in which a statistically significant association was observed between age ≥60 years and a higher probability of presenting adverse clinical outcomes (10). Similarly, a multicenter clinical trial conducted in the USA showed that heart failure patients aged 70 years or older had a 49% risk of hospitalization or mortality compared to 39.2% in those younger than 60 years (p value: <0.0001) (11). Likewise, some meta-analyses have associated age over 70 years with an increase in adverse clinical events (12-15).

Within BMI groups, overweight patients had a lower chance of adverse clinical outcomes. This is consistent with some research showing that patients with a diagnosis of heart failure and high BMI had lower adverse outcomes compared to other BMI groups, A possible explanation for the protective association of overweight in heart failure is the presence of greater metabolic and nutritional reserves that may improve tolerance to catabolic stress during decompensation episodes, as well as the secretion of adipokines with potential anti-inflammatory and metabolic effects (16-18). In contrast, an investigation in Iran found that patients with heart failure and high BMI had more adverse outcomes than underweight and normal weight groups (19). It is critical to understand the context of BMI within the obesity paradox. For example, Romero-Corral et al. point out a possible limitation in this interpretation, showing that the "obesity paradox" may be a false observation. In advanced stages of HF, unintentional weight loss related to cardiac cachexia and sarcopenia can displace frailer patients into lower BMI categories, generating reverse causation and inflating the apparent benefit of higher BMI (20). Another relevant aspect not to be overlooked is the role of intentional weight loss in patients with heart failure, which differs fundamentally from disease-driven wasting. Clinical trials in obese HF populations have shown that caloric restriction and supervised exercise programs significantly improve exercise capacity and quality of life (21).

Among the adverse clinical events evaluated, a statistically significant association was found between pulmonary hypertension and low BMI in heart failure patients. Similarly, a retrospective cohort performed in the USA evidenced that most patients with low BMI had PH and higher mortality compared to those with high BMI (22). However, in contrast to our findings, another retrospective cohort conducted at Massachusetts General Hospital reported a higher prevalence of pulmonary hypertension (69%) in overweight and obese patients living with HF (OR: 1.34; $p < 0.001$) (23). Likewise, Thayer TE et al. also identified an association between elevated BMI and an increased risk of developing pulmonary hypertension (OR > 1) (24).

The use of machine learning techniques in this study allowed the identification of relevant variables associated with adverse clinical outcomes. These findings support the potential role of advanced analytical approaches in improving risk stratification in heart failure populations (25, 26).

It is essential to recognize the limitations of the present study. First, the sample size was relatively small, which may limit the ability to detect statistically significant associations between BMI and clinical outcomes in patients with heart failure (27, 28). Therefore, we suggest extending the sample collection period for future research. Second, this study was conducted in a single tertiary-care hospital, which may introduce selection bias, since patients hospitalized in high complexity institutions usually present more comorbidities (29), which are clinically relevant variables frequently

associated with outcomes in HF, such as atrial fibrillation, chronic obstructive pulmonary disease, left ventricular ejection fraction, natriuretic peptides, sodium levels, and the use of guideline-directed medical therapy. Their omission may introduce potential residual confounding effects and limit the scope of interpretation. In addition, it is suggested that future studies consider a multicenter design that includes hospitals from different levels of care and regions of the country. An important limitation of this study is the use of a composite outcome, which includes clinically heterogeneous conditions. This approach may obscure differential associations between BMI and specific outcomes. It is possible that the observed effect is driven by the most frequent events rather than representing a uniform association across all complications. Additionally, the protective effect observed in overweight individuals may reflect reverse causation, were patients with more severe disease experience weight loss due to cachexia or sarcopenia. Furthermore, BMI does not differentiate between fat mass and lean mass, which limits its ability to accurately characterize nutritional status (30, 31). In subsequent studies, it is recommended to complement BMI with other tools such as bioimpedance skinfold measurements or, as implemented in a study conducted in Japan, body densitometry (DEXA) (32), as well as to standardize anthropometric measurement protocols. Additionally, absence of key heart failure variables such as left ventricular ejection fraction, NYHA functional class, natriuretic peptides, and pharmacological treatment may introduce residual confounding and limit the interpretation of the findings.

Finally, socioeconomic status was not measured int the present study which may influence nutritional status, access to health services, therapeutic adherence and clinical outcomes. Future studies should incorporate socioeconomic variables such as educational level, income, insurance status, and housing conditions that may act as confounders or effect modifiers. Despite these limitations, this study provides valuable regional evidence and highlights the need for further research using prospective designs, larger sample sizes and more precise measures of body composition.

Conclusions

The present study showed that the overweight category was associated with a lower probability of adverse clinical outcomes in patients with HF, partially supporting the existence of the obesity paradox in this population. Likewise, it was identified that older age was associated with a greater number of clinical outcomes. Furthermore, the presence of pulmonary hypertension was especially associated with the underweight group. These findings highlight the importance of considering variables such as age, BMI and comorbidities when stratifying clinical risk in patients hospitalized for heart failure. Nevertheless, further studies are required in our population, with a larger sample size, to validate or refute these results, as well as to explore in greater depth the clinical implications of this paradox in Latin American contexts.

Notes

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Conflicts of interest disclosure

The authors declare no competing interests relevant to the content of this study.

Authors' contributions

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve the version to be published.

Availability of data and responsibility for the results

All the authors declare to have had full access to the available data and they assume full responsibility for the integrity of these results.

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