

Original article

Influence of Obesity and Malnutrition on Acute Heart Failure

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ABSTRACT

Introduction and objectives: Obesity is an independent risk factor for the development of heart failure. Several recent studies have found better outcomes of heart failure for obese patients, an observation termed as the "obesity paradox." On the other hand, the negative effect of malnutrition on the evolution of heart failure has also been clearly established.

Methods: Data from the Minimum Basic Data Set were analyzed for all patients discharged from all the departments of internal medicine in hospitals of the Spanish National Health System between the years 2006 and 2008. The information was limited to those patients with a primary or secondary diagnosis of heart failure. Patients with a diagnosis of obesity or malnutrition were identified. The mortality and readmission indexes of obese and malnourished patients were compared against the subpopulation without these diagnoses.

Results: A total of 370 983 heart failure admittances were analyzed, with 41 127 (11.1%) diagnosed with obesity and 4105 (1.1%) with malnutrition. In-hospital global mortality reached 12.9% and the risk of readmission was 16.4%. Obese patients had a lower in-hospital mortality risk (odds ratio [OR]: 0.65, 95% confidence interval [95%CI]: 0.62-0.68) and early readmission risk (OR: 0.81, 95%CI: 0.78-0.83) than nonobese patients. Malnourished patients had a much higher risk of dying while in hospital (OR: 1.83 95%CI: 1.69-1.97) or of being readmitted within 30 days after discharge (OR: 1.39, 95%CI: 1.29-1.51), even after adjusting for possible confounding factors.

Conclusions: Obesity in patients admitted for HF substantially reduces in-hospital mortality risk and the possibility of early readmission, whereas malnutrition is associated with important increases in in-hospital mortality and risk of readmission in the 30 days following discharge.

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Influencia de la obesidad y la desnutrición en la insuficiencia cardiaca aguda

RESUMEN

Introducción y objetivos: La obesidad es un factor independiente de riesgo de insuficiencia cardiaca; sin embargo, se ha demostrado que los pacientes obesos con insuficiencia cardiaca tienen mejor evolución, lo que se ha llamado «paradoja de la obesidad». Por otro lado, la desnutrición tiene un papel pronóstico negativo en la insuficiencia cardiaca.

Métodos: Se analizaron los datos del Conjunto Mínimo Básico de Datos de los pacientes con diagnóstico de insuficiencia cardiaca dados de alta por todos los servicios de medicina interna del país en los años 2006-2008. Se identificó a los pacientes con diagnóstico de obesidad y/o desnutrición y se comparó la tasa de mortalidad y reingresos de los pacientes con desnutrición u obesidad con los que no las tenían.

Resultados: Se analizaron 370.983 ingresos por insuficiencia cardiaca; 41.127 (11,1%) tenían registrado un diagnóstico de obesidad y 4.105 (1,1%), de desnutrición. La mortalidad total fue del 12,9% y el riesgo de reingreso, del 16,4%. Los pacientes obesos presentaron menos riesgo de muerte durante el ingreso (odds ratio [OR] = 0,65; intervalo de confianza del 95% [IC95%], 0,62-0,68) y de reingreso a los 30 días (OR = 0,81; IC95%, 0,78-0,83) que los no obesos. Los pacientes con desnutrición tenían más riesgo de fallecer (OR = 1,83; IC95%, 1,69-1,97) o reingresar (OR = 1,39; IC95%, 1,29-1,51), incluso cuando se ajusta por posibles factores de confusión.

Palabras clave:

Insuficiencia cardiaca

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Obesidad

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Conclusiones: La desnutrición en los pacientes hospitalizados por insuficiencia cardiaca aumenta el riesgo de muerte durante el ingreso y la posibilidad de reingreso, mientras que la obesidad se comporta como un factor protector.

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Abbreviations

BMI: body mass index
 HF: heart failure
 OR: odds ratio

INTRODUCTION

Heart failure (HF) is a progressive disease that produces high rates of mortality and morbidity, along with high health costs. The risk factors independently associated with a higher risk of developing HF include obesity, arterial hypertension, and hypercholesterolemia. However, these 3 factors have in turn surprisingly been associated in several different studies with lower rates of morbidity and mortality in patients with HF.^{1,2} In recent years, many studies have indicated that in patients with acute processes and even chronic diseases, overweight/obesity acts paradoxically as a positive prognostic factor, when compared to patients with normal weight values; this is known as the “paradoxical effect of obesity” or the reverse epidemiology of conventional cardiovascular risk factors.^{3–11}

Several possible causes have been described to explain this epidemiological paradox, such as the higher metabolic reserve associated with greater weight, which allows these patients to face the acute decompensation from chronic diseases with a greater possibility of survival.^{2,12} It also has been reported that obese heart disease patients with HF have lower levels of N-terminal fragment of B-type natriuretic peptide than those with normal weight.^{13,14}

On the other hand, it has been clearly established that malnutrition is an independent prognostic factor for mortality in HF,¹⁵ which has led to the coining of the term “cardiac cachexia.”¹⁶ This process has also been related to the presence of tumor necrosis factor alpha (TNF-alpha),¹⁴ indicating that HF acts as a multi-systemic disease with chronic inflammation. The consequence of the circulating cytokines produced by these processes is damage to the digestive system, causing alterations in the intestinal barrier and dysfunctional protein transport¹⁷ along with increased intestinal permeability caused by increased bacterial translocation from the intestinal mucosae. These processes contribute to a poor absorption of nutrients in these patients, which in turn leads to malnutrition.¹⁸

In this study, we analyzed the influence of obesity and malnutrition on the mortality rate of patients admitted to internal medicine departments for acute decompensation produced by HF, as well as on the risk of a second hospitalization within 30 days for the same reason. We included all discharges of HF patients from internal medicine departments in Spain between 2006 and 2008.

METHODS

Data produced by the Minimum Basic Data Set were analyzed for patients diagnosed with congestive HF and discharged from

internal medicine departments as reported by all hospitals within the Spanish National Health System between 2006 and 2008, according to the Spanish Ministry of Health and Consumption. The Minimum Basic Data Set is a mandatory information system to which all hospitals must submit periodic reports, sent to the health department of the respective autonomous communities as well as the central Ministry of Health and Consumption. These databases utilize the coding system established by the International Classification of Diseases, 9th Revision Clinical Modification (ICD-9-CM). We grouped patient discharges by associated diseases according to the classification system of Diagnosis-Related Groups, version 21.0.

We selected cases of hospitalization with an HF code in the primary or secondary diagnosis (ICD-9-CM: 398.91, 404*, 402.11, 402.91, 428-428.9). We identified patients coded for obesity (ICD-9-CM: 278.00-278.09) or malnutrition (ICD-9-CM: 260-263.9) upon admission. We also identified the following risk factors: hypertension: ICD-9-CM 401.0, 401.1, 401.9, anemia: ICD-9-CM: 280.00-285.99, smoking: ICD-9-CM:305.10, alcoholism: ICD-9-CM:305.00-305.03, atrial fibrillation: ICD-9-CM: 427.3-427.32, myocardial infarction: ICD-9-CM: 410-410.9, ventricular dysfunction: ICD-9-CM: 429.9, dementia: ICD-9-CM: 290-290.9, diabetes: ICD-9-CM: 250.00-250.99, cancer: ICD-9-CM:140.0-172.9, 174.0-195.8, 200-208.9, V10.0-V10.9, chronic kidney failure: ICD-9-CM: 585-586.99, 582.0-582.9, 583.0-583.7, 588.0-588.9, and chronic obstructive pulmonary disease: ICD-9-CM: 416.8, 416.9, 500-505, 506.4, 490-496.

We used the Charlson index,¹⁹ which was developed in 1987 to demonstrate the relationship between comorbidity and 1-year mortality rates in different cohorts of patients. The index, which has been adapted for use in administrative databases,²⁰ evaluates the presence of 19 different medical conditions, with a weight of 1–6, and a total score that varies between 0 and 37. Any score higher than 2 corresponds to a 1-year mortality rate greater than 50%.

We performed a descriptive analysis of the data and compared demographic variables between patients who died during the episode and those who did not, as well as between patients readmitted to the hospital and those who were not. We used the chi-square test with the Yates correction for categorical variables, Fisher exact test for dichotomic variables when the expected value of a cell was less than 5, and Student t test for quantitative variables. We performed univariate analyses adjusting for age. The odds ratio (OR) and 95% confidence intervals (95%CI) were estimated using the regression coefficients. We also performed a multivariate analysis to determine whether obesity and malnutrition were independent variables of mortality and readmission of HF patients. To this end, we considered the dependent variables of mortality (model 1) and readmissions (model 2), and introduced the variables that resulted significant in the univariate analysis or had clinical significance as possible confounding factors; $P < .05$ was considered statistically significant. We used SPSS software version 15.0 for all statistical analyses.

RESULTS

We analyzed 370 983 cases of patients discharged with the diagnosis of HF during the 3-year study period. Mean patient age was 79.11 (10.13) years, and 55.1% were women. Of these patients,

45 429 died during hospitalization (12.2%). Within the 30 days following discharge, 61 008 patients were readmitted (16.4%). A total of 41 127 patients (11.1%) had a diagnostic code for obesity, and 4105 (1.1%) were classified as malnourished.

Table 1 summarizes the characteristics of HF patients diagnosed with obesity, those with malnutrition, and the general population. Obese patients were significantly younger (74.5 years vs 79.7 years, $P<.001$) and a higher percentage of obese patients than nonobese patients were women (66.4% vs 53.7%; $P<.001$), diabetic (52.1% vs 33.9%; $P<.001$), and smokers (5.5% vs 4.4%; $P<.001$).

Malnourished patients were older than properly nourished patients (81.3 years vs 79.7 years; $P<.001$), were hospitalized for a much longer period of time (17.8 days vs 10.4 days; $P<.001$), and had a higher frequency of diagnosis of neoplasia (10.4% vs 6.6%; OR: 1.75, 95%CI: 1.68-1.93; $P<.001$), dementia (12.4% vs 4.9%; OR: 2.95, 95%CI: 2.68-3.24; $P<.001$), and anemia (35.3% vs 20.7%; OR: 2.14, 95%CI: 2.01-2.29; $P<.001$).

Obese patients had a mortality rate 49% lower than nonobese patients (OR: 0.51, 95%CI: 0.48-0.52). The risk of readmission to the hospital was also 19% lower in obese patients (OR: 0.81, 95%CI: 0.78-0.83). Patients classified as malnourished had almost double the rate of mortality (OR: 2.29, 95%CI: 2.13-2.46) and a 36% higher risk of readmission (OR: 1.36, 95%CI: 1.26-1.46) than properly nourished patients. These trends were maintained even after the analysis was adjusted for possible confounding factors, such that after adjusting for sex, age, level of hypertension, diabetes, acute kidney failure, chronic kidney failure, anemia, ischemic cardiopathy, noninvasive ventilation, and other factors that increase mortality, such as dementia or neoplasia, obesity remains as a factor that decreases mortality rates (OR: 0.65, 95%CI: 0.62-0.68) and malnutrition as a risk factor for mortality (OR: 1.83, 95%CI: 1.69-1.97). In the risk analysis for readmissions, a similar trend was observed, resulting in a similar risk level even after correcting for other risk factors (Table 2).

DISCUSSION

This study demonstrates that obesity is associated with a significantly lower risk of death in patients hospitalized for HF, and that malnutrition in these patients doubles the risk of death during hospitalization. This relationship is independent of other prognostic factors that may influence the evolution of HF, such as age, sex, and certain comorbidities. Additionally, obese patients with HF that have been discharged from hospital have a 19% lower readmission rate than those in the normal weight class, whereas malnourished patients are 36% more likely to be readmitted for HF within 30 days after discharge than those with a normal weight.

Our results appear to confirm the existence of the so called "obesity paradox" in patients hospitalized for HF. Previous studies had already established this trend.^{6,21,22} Fonarow et al. reviewed the data from 110 000 patients from the Acute Decompensated Heart Failure National Registry⁶ and studied the influence of body mass index (BMI) on risk of death in patients with acute decompensated HF, observing that patients with higher BMI had lower in-hospital mortality rates. More obese patients also had higher comorbidities, but were also younger and had less severe systolic dysfunction, which could in part explain the lower mortality rates. In a recent meta-analysis, Oreopoulos et al. also reported the presence of these associated comorbidities as an explanation for the protective effect of obesity against mortality in patients hospitalised for HF.²³ The diagnosis of hypertension and/or diabetes mellitus in these patients would have led them to be evaluated, treated, and controlled by a doctor. These authors also identified other factors that could explain this effect, such as a lower incidence of tobacco use in obese patients, a lower incidence of previous myocardial infarction, and a better response to anti-hypertensive drugs. In an adjusted risk analysis, the authors concluded that obesity had a protective effect in HF. In our study, obese patients were younger, with more females, more hypertensive and diabetic patients, less prevalence of ischemic heart disease, and a higher percentage of smokers than the nonobese

Table 1
Demographic and Clinical Characteristics of Patients With Heart Failure and Obesity or Malnutrition

	HF	HF and obesity	HF and malnutrition
No. cases	325 915 (87.9)	41 127 (11.1)	4105 (1.1)
Age, years	79.7±9.9	74.5±10.5 ^a	81.3±10.4 ^b
Stay in days	10.4±9.9	10±8.4	17.8±17.3 ^b
Men	174 908 (53.7)	27 218 (66.4) ^a	2242 (54.6)
Mortality	41 599 (12.8)	2843 (6.9) ^a	987 (24) ^b
Readmission <30 days	54 235 (16.6)	5910 (14.4) ^a	863 (21) ^b
AHT	106 827 (32.8)	14 828 (36.2) ^a	1062 (25.9) ^b
Diabetes Mellitus	110 442 (33.9)	21 350 (52.1) ^a	848 (20.7) ^b
Ischemic cardiopathy	44 088 (13.5)	4681 (11.4) ^a	352 (8.6) ^b
Acute respiratory failure	86 500 (26.5)	13 880 (33.9) ^a	1223 (29.8) ^b
Chronic kidney failure	46 238 (14.2)	5026 (12.3) ^a	622 (15.2) ^b
COPD	107 119 (32.9)	15 203 (37.1) ^a	1102 (26.8) ^b
Anemia	67 490 (20.7)	6952 (17) ^a	1450 (35.3) ^b
Neoplasia	21 395 (6.6)	1448 (3.5) ^a	427 (10.4) ^b
Tobacco use	14 453 (4.4)	2255 (5.5) ^a	202 (4.9) ^b
Charlson >2	142 490 (43.7)	18 240 (44.5) ^a	1817 (44.3) ^b
Dementia	15 889 (4.9)	850 (2.1) ^a	507 (12.4) ^b
Noninvasive ventilation	3499 (1.1)	1080 (2.6) ^a	77 (1.9) ^b

AHT, arterial hypertension; COPD, chronic obstructive pulmonary disease; HF, heart failure. Data are expressed as no. (%) or mean±standard deviation.

^a $P<.05$ in comparison with nonobese HF patients.

^b $P<.05$ in comparison with nonmalnourished HF patients.

Table 2

Mortality and Readmission of Patients With Heart Failure That Had Obesity or Malnutrition Compared to Normal-Weight Patients

	Death		Readmission	
	Crude OR	Adjusted OR*	Crude OR	Adjusted OR*
Obesity	0.51 (0.48-0.52)	0.65 (0.62-0.68)	0.84 (0.82-0.87)	0.81 (0.78-0.83)
Malnutrition	2.29 (2.13-2.46)	1.83 (1.69-1.97)	1.35 (1.26-1.46)	1.35 (1.25-1.45)

OR, odds ratio (95% confidence interval).

*Adjusted for age, sex, risk factors (hypertension diabetes, tobacco use), ischemic cardiopathy, chronic kidney failure, acute respiratory failure, and possible confounding factors such as dementia and noninvasive ventilation.

group with this diagnosis. The greater proportion of smokers in obese patients in our study could possibly be explained by the fact that these patients were younger. However, a recent study performed in Spain demonstrated that smokers have a better prognosis than nonsmokers after a myocardial infarction,²⁴ although tobacco use appears to be associated with worse evolution in HF patients in some studies.²³ The presence of more cardiovascular risk factors in the obese population and their lower mortality rate make up the “protective paradox” of these risk factors. Although it is difficult to explain, researchers have pointed to the earlier treatment and therefore better medical control that these patients receive.^{21,22} For these same reasons, HF would appear earlier and with more severe symptoms in obese patients, but the disease would be less advanced, with a milder systolic dysfunction (as occurred in our study).^{22,25} In a study by Gustafsson et al. analyzing the influence of BMI on mortality in 4700 patients hospitalized for HF, BMI was correlated with left ventricular function and HF prognosis (survival was higher in patients with conserved left ventricular function and overweight/obesity than in sick patients below the normal weight range.) However, when ventricular dysfunction does exist, the mortality curve takes on a U shape and there is higher mortality at extreme weight classes,²⁶ as was later confirmed by other authors.²⁷ Additionally, obesity has not only been suggested to have a protective affect in acute decompensated HF patients, but also in those under outpatient follow-up, such as in the study by Zamora et al. with a Spanish cohort of 501 patients monitored for two years.²⁸ These same authors recently showed that this effect is maintained over notably longer periods of follow-up that reach 5 to 8 years.²⁹ In Spain, a second prospective follow-up study, in this case with 712 patients from internal medicine departments, taken from the Spanish registry of HF (*Registro Nacional de Insuficiencia Cardiaca*), showed that patients with a higher BMI had lower mortality rates, and that a higher BMI was associated with lower levels of human natriuretic peptide.³⁰ Our study is the first study in Spain in which the influence of obesity on in-hospital mortality has been demonstrated, showing that obese patients not only have a lower mortality rate while hospitalized, but also a lower rate of readmission.

The “obesity paradox” has also been described in other medical pathologies^{3,5} and surgical patients,⁹ such that higher mortality rates have been observed within the first month after surgery in malnourished and extremely obese patients, and lower rates in overweight and moderately obese patients, even when adjusting for risk factors such as hypertension and diabetes.¹¹

On the other end of the nutritional spectrum, malnourished patients admitted for HF were associated in our study with a notably high risk of death during hospitalization (twice as high as other patients) and a 36% higher rate of readmissions during the month following discharge. Malnutrition has previously been shown to be a negative prognostic factor.^{15,31-33} Malnutrition in HF is multifactorial, and is associated with reduced appetite, reduced intestinal absorption due to edema, and even the development of protein-losing enteropathy and chronic inflammation with high TNF-alpha levels in HF patients.³⁴ In contrast with malnourished

patients, obese patients have shown lower levels of TNF-alpha in the bloodstream because of their increased number of receptors in adipose tissue.³⁵

Hypoalbuminemia has been indicated as an independent prognostic factor associated with higher mortality in decompensated HF, and can be a result of malnutrition but also could be due to the increased catabolic activity, a dilutional state, chronic inflammation, and proteinuria in these patients.³⁶ The prevalence of malnutrition in HF patients is not well known, and has been estimated at 20% to 70%, depending on the criteria used.³³ In our study, the percentage of malnourished patients was much lower (1.1%), which is associated with the lack of reporting of this condition in internal medicine departments, as we discussed in an earlier publication.³⁷

Based on previous studies, we could explain our results by speculating that obese patients have a larger metabolic reserve and can thus contend with a catabolic stress such as a new exacerbation of HF better than the malnourished patients, who are much more vulnerable with their limited metabolic reserves.^{6,38} The chronic pro-inflammatory state that characterizes obese patients, which implies an increase in CRP and cytokines (TNF-alpha, interleukins 1 and 6) and an altered adipokine equilibrium (leptin, adiponectin, etc.) could paradoxically explain the better response to HF in these patients because of the similarity of this condition to the adaptive response produced by stress, in this case, decompensated HF. This, along with the greater metabolic reserve of these patients, could explain the lower mortality rate and number of readmitted patients with obesity and HF in our study. Malnourished patients are much more vulnerable to catabolic stress because of their lack of an adequate metabolic reserve,^{6,38} necessitating strategies to identify malnutrition in HF patients and provide an early nutritional support to treat this risk factor.³³ We find very interesting the reflection by Artham et al., who recommended caution when considering the obesity paradox “so as not to confuse a risk marker with a risk factor,” and pointed out that although obesity is a risk factor for the development of HF, the presence of obesity in these patients improves the evolution of the condition, at least on a short-term basis.³⁹

Among the limitations to this study, we must point out that the percentage of obese patients in our study (11.1%) was on the lower limit of the range described in the medical literature (15% to 35%^{2,21,26,40}), as well as the extremely low percentage of malnourished patients observed in our study (1.1%). In a recent study, we showed that the diagnosis of malnutrition is clearly underreported in discharge records from the internal medicine department. In prospective studies in which almost 50% of these patients are in a state of malnutrition, barely more than 1% of the discharge papers report this condition,³⁷ and it is very probable that obesity is also not expressly indicated in the patient's report. This is one of the limitations to this study derived from an administrative database.³⁷ We must also point out that we did not have access to BMI information, nor did we know specific information regarding the type and level of obesity, body composition, basic nutritional parameters, treatments administered to the patients, or patient evolution after 30 days of follow-up.

It has also been shown that a limitation of studies performed with databases such as the Minimum Basic Data Set is their lack of good correlation with the clinical patient data. However, our group examined this possibility and we were able to confirm very high correlation and reliability of the data when comparing administrative data with clinical databases,⁴¹ which has also been shown on the national level.⁴² On the other hand, this was an extremely large database, including all hospital discharge reports of patients with HF from internal medicine departments in Spain within a 3-year period, a total of over 370 000 records. Finally, we must point out that another limitation of this study was that it involved only patients admitted to internal medicine departments, with characteristics different from those that are normally treated by cardiologists, such as younger patients, predominantly male, with valvular or ischemic etiologies, and more severe systolic dysfunction, whereas those attended in internal medicine are generally older, female, and have a hypertensive etiology with preserved systolic function.⁴³

Our study is the first in Spain to show the protective effect of obesity on mortality and readmissions for HF, as well as the negative role played by malnutrition within these parameters; however, we wish to be cautious in establishing conclusions. Observational studies that have analyzed the obesity paradox in the follow-up of patients with HF have not established that weight loss is not beneficial for patients with ischemic cardiopathy, as could be inferred by our results.²⁴ We do believe that we can infer from our study that when obese patients are faced with a catabolic situation such as hospitalization for HF, they have a higher survival rate and better short-term evolution, which could be explained by the excess adipose tissue that would aid in neutralizing released cytokines and buffer the effects of the systemic inflammatory system.⁴⁴ On the other hand, more studies are needed to explore whether early detection of malnutrition in HF patients and implementation of corresponding nutritional treatment is accompanied by an improved evolution of these patients, since today we do not have sufficient evidence to recommend this course of action.³³

CONCLUSIONS

Our analysis of a large series of patients hospitalized for HF appears to confirm the protective effect of obesity, both in terms of mortality during hospitalization and in terms of need for readmission within 30 days following hospital discharge. We have also confirmed the important negative role played by malnutrition in these patients.

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CONFLICTS OF INTEREST

None declared.

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