# El peso de la insuficiencia cardíaca en un servicio de medicina interna en Portugal

The Burden of Heart Failure in an Internal Medicine Service in Portugal

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## **ABSTRACT**

**Introduction and Objectives:** Heart failure (HF) is a serious public health problem that involves high costs to healthcare services. Nevertheless, economic impact studies are absent. The aim of this study was to try to assess the cost of heart failure.

**Methods:** A retrospective observational study with statistical analysis was performed. The population of this study was the total number of hospitalised patients in an eight-month period with the primary diagnosis of HF. The variables were organised into groups: demographics, diagnosis, complementary diagnostic tests, pharmacological therapy, clinical data, procedures, professionals, and hospitalisation.

**Results:** The total expense was EUR 648,416.64 (EUR 4,103.90  $\pm$  2,563.36). The main cost was hospitalisation, which accounted for 44.67% of the total cost. In the parametric tests, a significant difference was identified between the autonomy of the patient, the decompensation cause, diabetes mellitus, creatinine clearance, and the number of days of internment. Only creatinine clearance presented a statistical difference when compared to the total cost.

**Conclusions:** Although several variables were tested, only creatinine clearance proved to directly influence the costs.

Keywords: Heart failure, cost, hospitalization.

#### RESUMEN

Introducción y objetivos: La insuficiencia cardíaca (IC) es un grave problema de salud pública que implica elevados costes para los servicios sanitarios. Sin embargo, no existen estudios de impacto económico. El objetivo de este estudio fue intentar evaluar el coste de la insuficiencia cardíaca.

**Métodos:** Se realizó un estudio observacional retrospectivo con análisis estadístico. La población de este estudio fue el total de pacientes hospitalizados en un período de ocho meses con diagnóstico primario de IC. Las variables se organizaron en grupos: demografía, diagnóstico, pruebas diagnósticas complementarias, terapia farmacológica, datos clínicos, procedimientos, profesionales y hospitalización.

**Resultados:** El gasto total fue de 648.416,64 euros (4.103,90) euros  $\pm 2.563,36$ ). El principal costo fue la hospitalización, que representó el 44,67% del costo total. En las pruebas paramétricas se identificó diferencia significativa entre la autonomía del paciente, la causa de la descompensación, la diabetes mellitus, la depuración de creatinina y el número de días de internación. Sólo el aclaramiento de creatinina presentó diferencia estadística respecto al coste total.

Conclusiones: Aunque se probaron varias variables, sólo el aclaramiento de creatinina demostró influir directamente en los costes.

Palabras clave: Insuficiencia cardíaca, costo, hospitalización.

## INTRODUCTION

Heart failure (HF) is a public health problem with high prevalence (nearly 26 million cases per year) and a high mortality rate. 1,2,3

In Portugal, the hospitalisation rate due to HF was 27.9/100,000 inhabitants, which corresponds to 182,512 days of hospitalisation and an average hospitalisation period of 9.8 days<sup>4</sup>. This rate is similar to that of diabetes mellitus (30.0/100,000 inhabitants), but HF has a higher gross mortality rate (12.9% in comparison with 5.1% for diabetes).<sup>4</sup>

It is estimated that HF represents a direct global cost of USD 65 billion and an indirect cost of 43 billion dollars<sup>5</sup> but the real cost of HF is unknown and underestimated. In Europe, the cost corresponds to 1–3% of the total healthcare costs, and the greatest part of the costs is due to hospitalisation (60–74%)<sup>2,6,7</sup>. In the United States of America, an annual cost of 34.4 billion dollars is estimated, with a probable increase of 127% in costs by 2030.<sup>2</sup>

There are only few studies<sup>7</sup> that address the direct cost of heart failure and the parameters that were analysed in the various studies focused on demographical characteristics and HF characterisation, resources (complementary diagnostic tests and pharmacological and human resources) and hospitalisation length.<sup>8,9,10</sup>

Urbich *et al.* (2020), in their review for the cost in United States of America, refers that the median cost for a HF-specific hospitalization was \$13,418 per patient and for patients with co-morbidities \$14,015 per patient. Olchanski *et al.* estimated mean hospitalization higher costs with diabetes with HFrEF (\$16,679) and HFpEF (\$15,301) status at admission.<sup>11</sup>

Stafylas *et al.* reported costs of EUR 5,589.66  $\pm$  4,560.03 (average cost EUR 4,565.30  $\pm$  4,379.79); Morgan *et al.* reported costs of EUR 10,474  $\pm$  2,478 (average cost EUR 6,068  $\pm$  1,681) and Sözmen *et al.* reported costs of TRY 2,350.8  $\pm$  3,202.9 (542.2  $\pm$  803.5).<sup>2,9,12</sup>

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Table 1. Diagnostic hypotheses.

DIAGNOSTIC HYPOTHESES		
Independent Variables (H0)	Dependent Variables (H1)	
Gender Autonomy Age Group NYHA Class (at admission) Cardiorenal Syndrome Ejection Fraction Aetiology Cause of Decompensation No. of Comorbidities Creatinine Clearance Diabetes Mellitus	Number of Days of Hospitalisation Total Cost of Complementary Diagnostic Tests Pharmacological Therapy Cost of Hospitalisation	

The difficult quantification of HF costs is a consequence of the absence of data on primary diagnostic costs; the undervaluation of the costs of technological and pharmacological treatments; and the devaluation of the influence of comorbidities on the costs, of the health professionals involved in HF treatment, and of the cost of the comorbidities.<sup>13</sup>

The present study aims to evaluate the direct cost of hospitalization for heart failure as the main diagnosis and to evaluate the factors that influence hospitalization and cost.

## **METHODS**

Quantitative, retrospective, and descriptive methodology was used. A literature review was performed to acquire and consolidate concepts and, subsequently, select the variables for the study. The databases that were used were B-on®, PubMed® and Scopus®, and the keywords that were used were "Heart Failure"; "Heart Failure" and "Economics"; "Heart Failure" and "Cost"; "Heart Failure" and "Burden"; and "Heart Failure" and "Microcosting". The study was approved by the hospital ethics committee and conforms to the ethical guidelines of the 1975 Declaration of Helsinki (Hospital approval number 10592/18-10-25).

The total period of study was 8 months. The location of the study was the Internal Medicine ward in a secondary hospital. The patients were identified using the International Classification of Disease -10 (ICD-10) coding system corresponding to the different HF presentations. The exclusion criteria were as follows: younger than 18 years, transfer to another hospital, abandonment, discharge against medical opinion, poorly coded process, hospitalisation period less than 24 h. Each episode represents one hospitalisation.

The variables were organised in groups as follows:

Demographic Characteristics; Diagnosis; Complementary Diagnostic Tests; Pharmacological Therapy (guideline-directed medical therapy in the treatment of HF with a depressed ejection fraction and non-directed medical therapy in the treatment of HF); Clinical Data; Procedures; Professionals and Hospitalisation.

The data was provided by auditing the patient's electronic clinical record (S-Clinico® and Alert®). The prices of the various variables were provided: by the pharmaceutical service (therapeutics), imaging service and laboratory (complementary diagnostic tests), by the Coding and Auditing Office (hospitalization and procedures). The value of the professionals was assigned by the cost per hour in the salary table (nursing – Salary table level 33, doctor – Salary table 40 h hospital assistant 5th position). In the case of medical costs, 1 hour per day was considered and in the case of nursing, 3 hours per day (1 hour per shift). A summation of the various variables was carried out.

Statistical analysis was performed by using the program Statistical Package for Social Sciences (SPSS) version 24®; p < 0.05 was the significance value in the statistical tests. The statistical tests were (when the assumptions of normal distribution, independence of samples and homogeneity were confirmed) independent T-tests and analysis of variance. The hypotheses are presented in groups (Table 1).

# **RESULTS**

The total number of hospitalisations in the Medicine ward was 1,188. HF as a main diagnosis corresponded to 13.3% of the hospitalisations (corresponding to 158 patients). The variables (Tables 2 and 3) were as follows:

The Total of Cost HF was 648,416.64 Euros (4,103.90  $\pm$  2,563.36 (Mean  $\pm$  Standard Deviation)) and with a daily cost 355.99  $\pm$  113.91 Euros (Mean  $\pm$  Standard Deviation).

The contribution of the various variables to the total cost was as follows: complementary diagnostic tests represented 15.55% of the total cost, procedures accounted for 14.27%, pharmacological therapy accounted for 4.41%, health professionals accounted for 18.02% and hospitality accounted for 44.67%.

In the parametric tests, a significant difference was identified between the number of days of hospitalisation and the following variables: autonomy of the patient (p = 0.017), the decompensation cause (p = 0.034), diabetes mellitus (p = 0.0469) and creatinine clearance (p = 0.007). Creatinine clearance (p = 0.007) showed a statistical differ-

Table 2. Description of hospitalised patients.

Variable	Value
Age	83.85 ± 7.64 years (mean and standard deviation)
Autonomy	Rankin 0–3: 62%
HF	Chronic (88.6%)
NYHA class (first evaluation)	NYHA IV (97.5%)
NYHA class (at discharge)	NYHA II (47.5%)
HF ejection fraction	HFmrEF (34.8%)
Aetiology	Coronary artery disease (24.7%) and arterial hypertension (24.1%)
Cause of decompensation	Infection (50.6%)
Number of comorbidities	5.96 ± 2.4 (mean and standard deviation)
Main comorbidities	Hypertension (88.6%), anaemia (61.4%), dyslipidaemia (50%)
Presence of cardiorenal syndrome	46%
Creatinine clearance	[45–60] mL/min (Mode)
Destination of the patients after medical discharge	Own domicile or domicile of relatives (51.9%), nursing home (36.1%),
Number of days in the hospital	12.7 ± 7.942 days (mean and standard deviation)
Mortality	5.1%

Table 3. Description of the costs.

COSTS OF COMPLEMENTARY DIAGNOSTICS, DRUGS, PROCEDURES AND PROFESSIONAL EXAMS			
Variable	Mean ± Standard Deviation (€)	Total (€)	
Cost of analyses	528.12 ± 318.85	8,1867.87	
Daily cost of analyses	51.41 ± 31.47	8,123.51	
Cost of imaging exams	112.89 ± 124.33	1,7836.89	
Total cost of complementary exams	638.34 ± 392.02	100,858.04	
Total daily cost of complementary exams	61.84 ± 34.68	9,771.21	
Cost of pharmacotherapy	181.14 ± 254.62	2,8619.94	
Cost of guideline-guided pharmacotherapy for HF	14.2210 ± 76.98	2,247.40	
Cost of other drugs	165.71 ± 214.83	2,6183.50	
Cost of procedures	708.89 ± 492.90	112,004.45	
Cost of transfusion erythrocyte concentrate	37.55 ± 148.21	5,932.25	
Cost of doctors	222.50 ± 148.34	35,155.11	
Cost of nurses	517.05 ± 348.35	81,693.47	
Cost of hospitality	1,750.05 ± 1296.63	276,507.85	

ence when compared to the total cost. *Post hoc* analysis showed that for the creatinine clearance classes, the statistical difference was, on average, between class 30 and 45 and >60 mL/min/1.73 m<sup>2</sup> (Table 4).

# **DISCUSSION**

It is almost impossible to compare the cost of HF. There are few studies on the topic, and these studies involve different parameters, different national health systems, different internal products and different forms of acquisition of services.<sup>2,9,10,13</sup>

The average cost of hospitalisation for HF was EUR 4,103.90  $\pm$  2,563.36, and the total cost was EUR 648,416.64 (average cost was EUR 1,750.05  $\pm$  1,296.63). However, the real cost of hospitalisation is likely to be higher because some variables could not be included in this study (e.g., assessment by other professionals, cost of oxygen therapy).

Stafylas *et al.* reported costs of EUR 5,589.66  $\pm$  4,560.03 (average cost EUR 4,565.30  $\pm$  4,379.79); Morgan *et al.* reported costs of EUR 10,474  $\pm$  2,478 (average cost EUR 6,068  $\pm$  1,681) and Sözmen *et al.* reported costs of TRY 2,350.8  $\pm$  3,202.9 (542.2  $\pm$  803.5). The study by Morgan *et al.* was the only with the values that were lower than those of HDG

RESULTS PARAMETRIC TEST - HYPOTHESIS GROUP		
Variable Sex	Variable Etiology	
Independent-samples T test (t)	Anova	
-1,597	0,427(Welch's)	
-1,069	0,598	
-2,44	0,273 (Welch's)	
-1,127	0,352	
Variable Autonomy	Variable Cause of Decompensation	
Independent-samples T test (t)	Anova	
0,017	0,034	
0,414	0,136	
1,022	0,227	
-0,192	0,733	
Variable Class Age	Variable Number of Comorbilities	
Anova	Anova	
0,822	0,845	
0,350	0,742	
0,613	0,783	
0,867	0,795	
Variable NYHA (at admission)	Variable Clearance de Creatinine	
Independent-samples T test (t)	Anova	
-0,145	0,007	
-1,070	0,420	
0,509	0.05 (Welch's)	
-0,245	0,007	
Variable Cardiorrenal Syndrome	Variable Diabetes Mellitus	
Independent-samples T test (t)	Independent-samples T test (t)	
-1,965	0,046	
0,530	0,498	
-1,388 (Welch's )	-1,126	
-1,363	0,164	
Variable Ejeccion Fraction		
Anova		
0,837		
0,396		
0,269		
0,605		

Table 4. Results parametric test - Hypothesis Group

in the country of study. Although we cannot perform a direct comparison, the standard deviation is high in all the studies. This variability may reflect the lack of protocols in the approach for HF and, subsequently, an increase in the costs.<sup>2,9,10,12</sup>

In terms of the contribution of the costs for heart failure, the length of hospitalisation represents the highest cost of heart failure in all the studies. It is important to implement strategies, such as outpatient programs and specialised inpatient programs to reduce the length of the hospital stay and, consequently, the associated costs.<sup>2,9,10,12</sup>

The mean cost of pharmacological therapy was EUR 181.14  $\pm$  254.62 (cost of guideline-guided pharmacotherapy for HF was EUR 14.221  $\pm$  76.98, and of the non-guideline-guided therapy for HF was EUR 165.71  $\pm$  214.83). In the analysis by Stafylas *et al.*, the average cost of pharmacological therapy per patient was EUR 618.91. Morgan *et al.* reported a cost of EUR 87  $\pm$  16, Sözmen *et al.* TRY 365.0  $\pm$  541.4 and Bierman *et al.*, a cost of EUR 290 was presented.<sup>2,9,12,14</sup>

According to Sözmen *et al.*, the cost of cardiovascular medication varies widely across different European countries (EUR 30 in Spain and

EUR 1.557 in the United Kingdom, which is between 2% and 31% of the percentage of the total cost of HF in each country). This discrepancy may be due to the heterogeneity of therapies implemented in different countries, different criteria in the inclusion of medicines considered for HF, or due to the inclusion of only medicines targeting HfrEF<sup>12</sup>. In this study, it was observed that the largest percentage of costs for drugs corresponds to drugs that are not guideline-guided for HF, that is, pharmacological therapy directed to the comorbidities and causes of decompensation. Another gap in the previous studies (and that has been bridged by this one) is the absence of an evaluation of the pharmacological therapy not directed to HF. A direct comparison of costs with other studies was not possible.

The procedure most frequently mentioned in several studies is the transfusion of red cells, because of the high quality and safety criteria associated with this procedure. The transfusion of red cells costs a mean EUR 37.55  $\pm$  148.21. Morgan *et al.* presented costs of EUR 123  $\pm$  77, and Sözmen *et al.* presented costs of TRY 551.9  $\pm$  798. The difference in cost may be related to the preference for the transfusion of red cells instead of intravenous iron in the treatment of iron deficiency anaemia or the presence of non-anaemic iron deficiency.  $^{9,12}$ 

Anaemia and HF are associated with a higher use of resources and higher costs. Reed *et al.* showed that, although there was no significant difference between HF patients with and without anaemia, there was a difference in the cost per year of USD 2.780 per patient, suggesting that anaemia may be an independent prediction factor of resource use.<sup>15</sup>

In the statistical analysis performed, there was no difference between male and female patients in terms of the length of the hospital stay, the cost of complementary diagnostic tests, total cost of the medicines, or total cost. This result is consistent with studies by Morgan *et al.* and Ku *et al.* According to Ku *et al.*, the lack of difference between male and female patients in this aspect may be due to a similar incidence of the pathology in both genders.<sup>6,9</sup>

Regarding autonomy, it was found that there was a significant difference between the level of autonomy and the length of the hospital stay (p = 0.017). It was not possible to conduct a comparative stud. Rankin 4–5 had a higher number of days of hospitalisation (total no. 1,197), which was possibly related to a higher number of comorbidities and need for medical care.

There was no statistical difference between age (organised in age classes for statistical evaluation) and the variables tested. In the study by Morgan *et al.*, patients younger than 65 years had significantly higher costs compared to patients older than this age. This finding suggests that younger patients would possibly be subjected to more aggressive therapies and complementary diagnostic tests and, therefore, be more expensive, which was also the conclusion presented by Smith *et al.*<sup>9,16</sup>. In this study, the number of patients younger than 65 years was very low. On the other hand, Ku *et al.* showed that there was no significant difference between age classes after controlling for risk factors<sup>6</sup>, but Lee *et al.* highlighted an increase in costs associated with increasing age due to comorbidities.<sup>17</sup>

As for NYHA class (at admission), there was no significant difference in the variables tested. In a study by Bierman *et al.*, a 71% increase in costs was observed between NYHA class I and NYHA class IV, but the

study included outpatients and did not perform a hypothesis test on the collected data. Stafylas *et al.* also demonstrated an increase in costs in higher NYHA classes<sup>2,13</sup>. In the model presented by Liao *et al.*, the NYHA classes III—IV were associated with a 41% increase in costs<sup>18</sup>. The lack of a significant difference between NYHA classes can be explained by the predominance of NYHA class IV in the study.

There is no cost assessment of cardiorenal syndrome. The literature that was reviewed for this study focuses on the evaluation of creatinine clearance and chronic kidney disease. For the independent variable of cardiorenal syndrome, a significant difference was found between the creatinine clearance and the number of hospitalisation days (p = 0.007) and the total cost (p = 0.007). *Post hoc* analysis showed that for the creatinine clearance classes, the statistical difference was, on average, between class 30 and 45 and >60 mL/min/1.73 m². Ku *et al.* showed an increase in cost with a decrease in creatinine clearance and with chronic kidney disease, as did Stafylas *et al.* and Liao *et al.*<sup>2.6,18</sup>

As for the ejection fraction, there was no statistically significant difference in the variables tested. The study by Smith *et al.* pointed to a lower cost in HF patients with reduced ejection fraction. Smith *et al.* pointed out that the higher cost may be related to the severity of the presentation or to the chronicity of the disease and not to the ejection fraction. In return, Stafylas *et al.* mentioned significantly lower costs for patients with a preserved ejection fraction compared to those with reduced ejection fraction HF. The study by Olchanski *et al.* also found lower costs for patients with preserved ejection fraction HF (although there was no significant difference). Further studies are needed to understand which value of the ejection fraction is responsible for higher costs during hospitalisation.<sup>2,8,16</sup>

The variable aetiology did not show a significant difference in relation to the variables tested. Although the clinical approach varies by aetiology, this study did not show significant differences between aetiologies. There are few researchers that link cost and aetiology, and those that have done evaluate only the cardiovascular aetiology, with the exception of Liao *et al.*, who demonstrated an increase in cost (31%) for coronary artery disease, but no significant difference in other aetiologies.<sup>18</sup>

The cause of decompensation was categorised into two options (cardiac causes vs. other causes), which showed a statistically significant difference across the number of days of hospitalisation (p = 0.034). The *post hoc* analysis (p = 0.048) showed that there was a significant difference between cardiovascular causes and the variable "other causes" (which are predominantly non-cardiovascular causes).

Due to the pooling of the variables, it is not possible to identify a single cause of decompensation that is responsible for the increase in the length of the hospital stay. In the literature that was reviewed for this study, there were no studies on the causes of decompensation and HF costs.

There was no significant difference in the number of comorbidities. Ku *et al.* refered a significant increase in costs associated with comorbidities such as chronic kidney disease and diabetes mellitus. In contrast, Morgan *et al.* highlighted an increase in the costs for patients without comorbidities (e.g., atrial fibrillation), possibly because they are subject to more aggressive treatments and diagnoses.<sup>9</sup>

In this study, a statistical analysis of diabetes mellitus was performed, and a significant difference was found in terms of the number of days of hospitalisation (p = 0.048). The result is similar with the study conducted by Bogner *et al.*, who reported an average cost increase of about USD 10.446 in patients with HF and diabetes mellitus compared with patients with only HF<sup>19</sup>. Olchanski *et al.* estimated mean hospitalization higher costs with diabetes with HFrEF (\$16,679) and HFpEF (\$15,301) According to Bogner *et al.*, the cost increase was due to the increase in the number of days of hospitalisation resulting from complications linked to diabetes<sup>19</sup>. Dunlay *et al.* refers to diabetes mellitus as a prediction factor for increases in HF cost throughout a lifetime.<sup>13</sup>

The main weaknesses of this work are: short time of the study, it evaluates only a hospital and a specific service, not distinguishing the cost of the internment and re-internment of the patients, it does not make any reference to the social costs, there is not a differentiation of the costs that are not related to HF, there is not an evaluation of the costs with the comorbidities, some specific costs are absent (e.g.: intravenous accesses), and in some variables the average value was considered (e.g.: health professionals).

# **CONCLUSIONS**

It is not possible to draw conclusions from comparisons with other studies due to the different methodologies, health systems and approaches to the different problems that are used in the different studies. Although the autonomy of the patient, the cause of decompensation and the presence of diabetes mellitus may influence the number of days of hospitalisation and, indirectly, its cost, that association has not been proven. The only factor that influenced the global cost was creatinine clearance.

## **CONFLICT OF INTEREST**

The authors declare that they have no conflict of interests.

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This research had no funding sources.

## ETHICAL ASPECTS

All participants submitted a consent form to be included in this study.

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