# Mortality After the First Hospital Admission for Acute Heart Failure, De Novo Versus Acutely Decompensated Heart Failure With Reduced Ejection Fraction

Raquel López-Vilella MD

*Heart Failure and Transplant Unit, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

Pablo Jover Pastor MD

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

Víctor Donoso Trenado MD

*Heart Failure and Transplant Unit, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

Ignacio Sánchez-Lázaro PhD

*Heart Failure and Transplant Unit, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain*

Eduardo Barge Caballero PhD

*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain*

*Cardiology Department, Complejo Hospitalario Universitario de A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain*

*Grupo de Investigación Cardiovascular (GRINCAR), Universidad de A Coruña (UDC), A Coruña, Spain*

María Generosa Crespo-Leiro PhD

*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain*

*Cardiology Department, Complejo Hospitalario Universitario de A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain*

*Grupo de Investigación Cardiovascular (GRINCAR), Universidad de A Coruña (UDC), A Coruña, Spain*

Luis Martínez Dolz PhD

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain*

Luis Almenar Bonet PhD

*Heart Failure and Transplant Unit, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Cardiology Department, University and Polytechnic Hospital La Fe, Valencia, Valencia, Spain*

*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain*

*Department of Medicine, University of Valencia, Valencia, Spain*

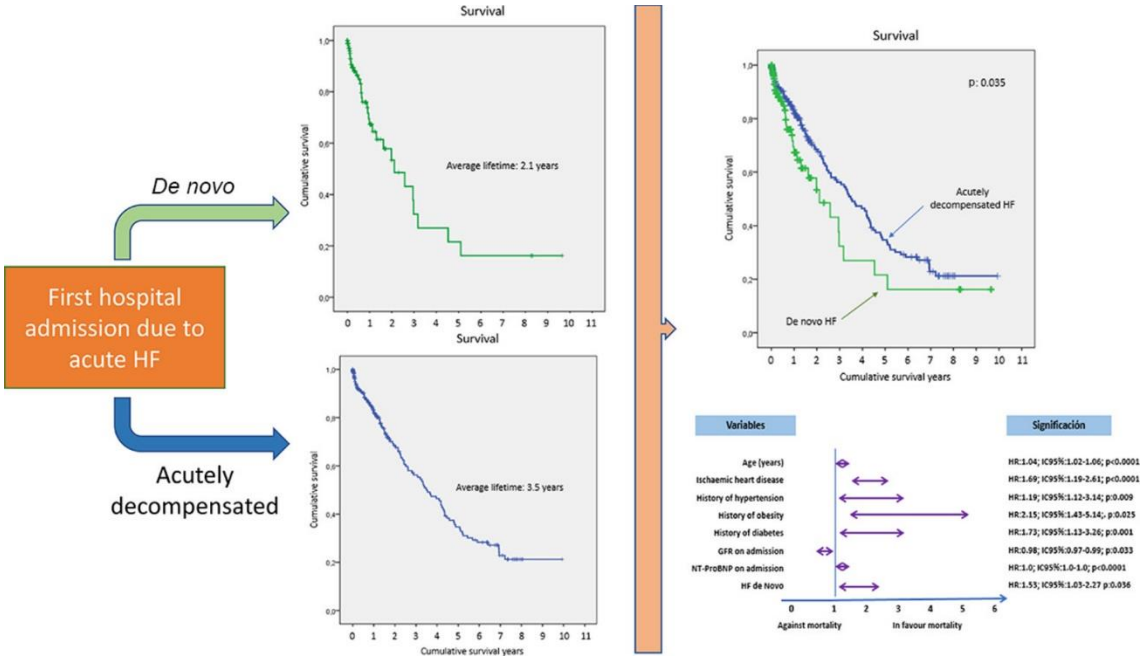
Corresponding author: Tel: +34961245851; fax:+34961246238. E-mail address: lopez_raqvil@gva.es (R. Lopez-Vilella).

**Abstract**

It is not clear to date whether a first admission in heart failure (HF) marks a worse evolution in patients not previously diagnosed with HF ("de novo HF") than those already diagnosed as outpatients ("acutely decompensated HF"). The aim of the study was to analyze whether survival in patients admitted for de novo HF differs from the survival in those admitted for a first episode of decompensation but with a previous diagnosis of HF. This study includes an analysis of 1,728 patients admitted for decompensated HF during 9 years. Readmissions and patients with left ventricular ejection fraction ≥50% were excluded (finally, 524 patients analyzed). We compared de novo HF (n = 186) in patients not diagnosed with HF, although their structural heart disease was defined, versus acutely decompensated HF (n = 338). The clinical profiles in both groups were similar. The de novo HF group more frequently presented with normal right ventricular function, with less presence of severe tricuspid regurgitation. The probability of survival was low in both groups. Thus, the median life in the de novo HF group was 2.1 years and in the acutely decompensated HF group, 3.5 years. There was a lower probability of long-term survival in the de novo HF group ($p = 0.035$). The variables associated with mortality were age ($p < 0.0001$), ischemic heart disease ($p < 0.0001$), hypertension ($p = 0.009$), obesity ($p = 0.025$), diabetes ($p = 0.001$), and N-terminal pro-brain natriuretic peptide at admission ($p < 0.0001$). A higher glomerular filtration rate was associated with better survival ($p = 0.033$). De novo HF was

associated with a higher mortality than chronic HF with acute decompensation (hazard ratio 1.53, 95% confidence interval 1.03 to 2.27, p = 0.036). In conclusion, the first admission for HF decompensation in patients with no previous diagnosis of HF identifies a subgroup of patients with higher long-term mortality.

**Graphical abstract**




Heart failure (HF) is a chronic disease with a negative and progressive continuum toward a worse functional and vital status of the patient. This progression is episodically interrupted by decompensations that make the disease progress more rapidly and aggressively.[1-3] Thus, hospitalizations because of decompensation, particularly the first decompensation, mark the beginning of a progressive deterioration that eventually leads to the patient's death. Previous studies do not clarify whether this first admission marks a worse evolution in patients not previously diagnosed with HF ("de novo HF") than those already diagnosed as outpatients ("acutely decompensated HF") and whether the clinical profile of both groups is similar. The hypothesis of this study was that patients who experience a first HF decompensation leading to hospital admission and who had not been diagnosed with HF would have a better prognosis than patients who were already diagnosed as outpatients and who experienced a first acute decompensation of their

disease. Thus, the aim of the study was to analyze whether the survival in patients admitted to hospital for de novo decompensated HF is different from those admitted for a first episode of decompensation but with a previous diagnosis of HF.

## Methods

This is a retrospective analysis on the prospectively completed database of consecutive patients hospitalized with a diagnosis of acute HF from June 2012 to June 2021. A total of 1,728 patients were recruited. Patients with preserved left ventricular ejection fraction (LVEF) and subsequently readmissions were excluded. Thus, only the first episode of HF decompensation leading to hospital admission was considered. The total number of patients included in the analysis was 524 (Figure 1).

The diagnosis of de novo HF was made when the patient was admitted for decompensation but had never been diagnosed with HF before, despite having cardiovascular risk factors or various heart diseases. The diagnosis of acutely decompensated HF was made when the patient had been diagnosed with HF on an outpatient basis but had never been admitted for acute decompensation. The 2021 European Society of Cardiology HF guidelines[4] were followed for the diagnosis of HF.

Clinical, electrocardiographic, echocardiographic, and pharmacological variables were analyzed. In terms of history, patients were considered hypertensive, dyslipidemic, diabetic, or hypothyroid when they were taking drugs to control these risk factors. Smoking was defined as being an active smoker or had not stopped smoking for <10 years. Alcoholism was defined as having a mean daily consumption of more than 20 g in women and 40 g in men and obesity was defined as having a body mass index was >35. Renal dysfunction was considered when the glomerular filtration rate was <60 and peripheral vascular disease when there were symptoms related to this vascular problem.

Left ventricular function depression was grouped depending on the LVEF into mild (40% to 50%), moderate (30% to 40%), and severe (<30%). Right ventricular function was estimated qualitatively. The right ventricle was considered dilated when the baseline diameter was >40 mm. The diagnosis of left ventricular hypertrophy was made when the interventricular septum and/or posterior wall was >12 mm. The limit of normality of the left atrium was 40 mm and of the left ventricle in end-diastole 56 mm. For the

diagnosis of valve disease severity, the European Society of Cardiology valvulopathy recommendations[5] were followed.

The study was conducted in accordance with the Declaration of Helsinki. The research project was approved by the Biomedical Research Ethics Committee of the Hospital University and Polytechnic Hospital La Fe, Valencia.

Categorical variables are expressed as percentages and numerical variables as mean ± SD or median with the interquartile range in case of $p < 0.05$ compared with the Kolmogorov Smirnov *Z*-test for normality. A comparative analysis was performed with chi-square test with Yates correction when the cases were few in any subgroup and the Student's *t* test or Mann–Whitney *U* test in the case of non-normal distribution for independent samples. For the univariate analysis of survival, Kaplan–Meier curves were used, comparing the curves by the log-rank method. For the multivariate analysis, Cox regression was used, introducing the variable "exitus" as the dependent variable. The independent variables were entered by blocks (clinical profile, diagnostic tests, analytical tests, and treatments) using the conditional regression method.

A value of $p < 0.05$ was considered significant. The statistical programmes used were IBM SPSS Statistics Version 27 and Stata Statistics/Data analysis 16.1 serial number 501606323439. The statistical programmes used were SPSS v.27.0 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. IBM Corp, Armonk, NY) and Stata Statistics 16.1 (StataCorp. 2019. Stata Statistical Software: Release 16. StataCorp LLC, College Station, TX)

## Results

Of the 524 patients included in the study during the 9-year inclusion period, 35.5% met the definition of de novo HF and 65.5% met the diagnosis of acutely decompensated HF. Comparing both clinical profiles, it was striking that they were quite similar groups, with not too many differences between them. However, it could be discerned that the patients admitted with a diagnosis of de novo HF were more obese and the most frequent cause of decompensation was a rapid supraventricular arrhythmia, such as atrial fibrillation (AF) or a hypertensive crisis. On arrival at the emergency department, they usually have a higher heart rate. In contrast, the reason for heart disease decompensation in patients with acutely decompensated HF is usually acute ischemic heart disease. In both types of

heart disease, infection as a cause of hemodynamic decompensation is close to 25% (Table 1).

The de novo HF group showed a higher incidence of AF/flutter on admission. In contrast, the acutely decompensated HF group showed higher degrees of depressed right ventricular function and tricuspid regurgitation. Comparing the analytical parameters at admission, there were few differences between the 2 groups. However, plasma urea and uric acid levels were higher in the acutely decompensated HF group (Table 2).

Multiple significant differences were found in the outpatient treatment that the patients were on at admission. Thus, patients with acutely decompensated HF were treated with HF prognostic modifying drugs, such as loop diuretics, antiarrhythmics, digoxin, and allopurinol. In contrast, patients with de novo HF were more frequently on nitrates and calcium antagonists (Table 3).

In our analysis, we referred to the overall mortality. There were 36% of deaths, 61% of which were cardiovascular. The survival function showed that in both groups, the reduction in survival was very high. Thus, the half-life (50% survival probability) in the de novo HF group was only 2.1 years and in the acutely decompensated HF group, 3.5 years. It could also be observed that the survival curves are very significantly reduced already at the beginning of admission. Comparing both curves showed that mortality was significantly higher in the de novo HF group (Figure 2). The multivariate analysis showed variables with significant statistical power to increase mortality: age, ischemic heart disease, history of hypertension (HT), obesity, diabetes mellitus, and the N-terminal pro-brain natriuretic peptide (NT-ProBNP) value at admission. In contrast, a higher glomerular filtration rate was associated with better survival. The diagnosis of de novo HF increased the probability of death during follow-up by a factor of 1.5 compared with acutely decompensated HF (Figure 3). Graphical abstract groups the graphical representation of survival outcomes.

## Discussion

HF is a highly prevalent disease that causes high morbidity and mortality, with frequent decompensations that accelerate the poor prognosis. The first admission has special connotations because the subsequent evolution throughout the follow-up may be different, depending on whether the patient has already been diagnosed with HF or

not.[1,2] There is much controversy in previous studies in this regard, with often contradictory data. In this study, it was observed that the majority of patients admitted for the first time had already been diagnosed with HF (65%); however, the profile between the 2 study groups was quite similar, except for treatment. A lower probability of survival was observed in patients with de novo HF, and an increased risk of mortality adjusted by a 1.5-fold increase in the probability of death at follow-up.

Traditionally, HF has been classified into 2 main groups: chronic HF and acute HF. The latter group can be further divided into 2 subgroups: de novo HF and acutely decompensated HF(nonde novo).[1-3] The vast majority of studies consider de novo HF to be those cases admitted with a diagnosis of acute HF without a previously known heart disease.[4,5] In contrast to what is described in previous studies, in our study, the de novo HF group is composed of patients with no previous diagnosis of HF, regardless of whether or not they had a previously known heart disease. An example of this is patients with a history of chronic ischemic heart disease who had never developed a previous clinical HF. This difference in terminology probably explains many of the differences found between this study and other previous studies.[6-8]

From a clinical point of view, no major differences were found comparing the 2 study groups. In fact, the clinical profiles are similar in terms of age, gender, cardiovascular risk factors, and underlying heart disease. The differences observed were that obesity and stroke were more frequent in the de novo HF group, whereas previous cardiac surgery, hypothyroidism, and atrial arrhythmias (fibrillation/flutter) were more frequent in the acutely decompensated HF group. However, differences were observed in the cause of decompensation, with decompensation because of arrhythmias or hypertensive crisis being more frequent in de novo HF and acute ischemic heart disease in acutely decompensated HF. These results differ from those reported in other studies, such as that of Raffaello et al,[6] which described ischemic events as the main cause of decompensation in de novo HF, whereas infections were the main cause in the acutely decompensated HF group.[6,9-11] Similarly, they also report differences in terms of underlying heart disease, with HT being more frequent in de novo HF, and co-morbidities, such as HT, diabetes mellitus, ischemic heart disease, chronic obstructive pulmonary disease, AF, and stroke, being more frequent in acutely decompensated HF. Moreover, in the acutely decompensated HF group, patients were older and more often had a history of infarction

and coronary revascularization.[6,7,10,12,13] In a similar vein, the meta-analysis by Pranata et al[8] found that patients in the de novo group were younger and had a lower prevalence of classic risk factors and co-morbidities than the non-de novo HF group. They also observed that acute coronary syndrome and hypertensive heart disease were more frequent in the de novo HF group, whereas valvular heart disease was more frequent in the acutely decompensated HF group.[8] As previously mentioned, the differences found in our study are probably explained by the difference in the definition of de novo HF because many of the patients classified as known HF in the presented studies would be part of the de novo HF group in our study.

Regarding the treatment differences, as would be expected, the acutely decompensated HF group had a higher percentage of patients receiving targeted HF medication, both prognostic modifying drugs and diuretics. There were no differences in the use of angiotensin-converting enzyme inhibitors or thiazides, probably related to the use of these drugs as antihypertensive therapy, because no differences were found between the groups with respect to HT. The higher use of digoxin and antiarrhythmic drugs in the acutely decompensated HF group is probably explained by the higher prevalence of atrial arrhythmias in this group. Of note, the small percentage of patients with de novo HF taking neprilysin and angiotensin II inhibitors probably did so because of the presence of previous ventricular dysfunction. The comparison of treatment between the 2 groups shows that patients with de novo HF have considerable percentages in the use of cardiovascular treatments, some of them even higher, as in the case of nitrates and calcium antagonists, which shows that they are not naive patients from a cardiovascular point of view, as is the case in other studies.[14-15]

At the analytical level, no significant differences were found in most parameters except for urea and uric acid, which were higher in the de novo HF group. These results contrast with those found in previous studies, where lower hemoglobin levels and higher creatinine and NT-ProBNP levels have been observed in the acutely decompensated HF group.[6,16-17] A meta-analysis also found overall that NT-ProBNP levels are lower in the de novo HF group[6]; although, there are studies in which no differences were found.[12] The absence of analytical differences in our study is probably related to the absence of differences in the clinical profile of the patients.

Although patients with acutely decompensated HF had a lower prevalence of known AF, these patients had a higher rate of AF as a rhythm on admission. These results are consistent with those reported by other groups in which this arrhythmia was also predominant in this group.[8,18]

Regarding echocardiographic findings, in our results, we found no major differences between the 2 study populations. Significant differences were found only in the presence of tricuspid regurgitation and higher rates of right ventricular systolic dysfunction in the acutely decompensated HF group. These results contrast with those of other studies in which a lower LVEF has been found in known HF[14,19-21]; although, other registries, similar to ours, found no significant differences in LVEF.[22,23]

As is well known, admission for HF determines the prognosis of the disease. The question we asked ourselves was to assess whether the prognosis was the same for patients with and without a previous diagnosis of HF after a first admission for HF. We observed that the mean survival of the de novo HF group was 2.1 years compared with 3.5 years for the acutely decompensated HF group, with significant differences. Thus, in patients admitted for the first time, without a previous diagnosis of HF, the probability of death during follow-up was 1.5 times higher. Thus, our results describe a worse prognosis in patients admitted for the first time without a previous diagnosis of HF. In addition, variables associated with increased mortality were age, ischemic underlying heart disease, HT, diabetes mellitus, obesity, and NT-ProBNP on admission. In contrast, a higher glomerular filtration rate was associated with better survival. On the one hand, similar results have been described in previous studies for the variables associated with a higher mortality on the first admission for HF, such as age, blood pressure, right ventricular dysfunction, others, such as sodium and urea levels in the blood, and LVEF.[24-26] Our results contrast with those described so far in most published studies, which describe a higher mortality in the acutely decompensated HF group,[12,14,27,28] which has been related to older age and the presence of co-morbidities in this group.[29] Although these results may seem surprising, there are actually contradictory data in previous studies, and therefore, the prognosis of these patients remains a matter of debate. However, there are also studies in which no differences in 1-year mortality were found between the 2 groups.[14,20]

Thus, after an analysis of both groups of patients, the initial hypothesis, based on the results described in previous studies, is not confirmed. In this hypothesis, it was

considered that patients with a previous diagnosis of HF would have a worse prognosis because, despite being treated for HF, they decompensated to such an extent that they had to be hospitalized. However, this has not been the case; in patients with no previous diagnosis of HF, the long-term prognosis is worse, perhaps in relation to the lower prescription of prognosis-modifying drugs for HF when they decompensate. This fact allows us to theorize whether available HF drugs should be administered to all patients with myocardial dysfunction even if they are asymptomatic and irrespective of ejection fraction (the Studies of Left Ventricular Dysfunction clinical trial already demonstrated that this treatment does add benefit in asymptomatic patients with reduced ejection fraction).[30]

Our results are possibly influenced by our novel definition because the vast majority of studies refer to de novo patients as patients without a previous heart disease. Therefore, this study provides a different and novel point of view, which makes it particularly relevant. The most important limitation of this study is the inherent limitation of the patient registry databases. However, it presents a fairly accurate method because the data were entered prospectively as patients were admitted and by the same person, which confers reliability, avoiding biases between patients. In contrast, the recruitment time was 9 years, which sufficient to obtain a significant number of patients. It is important to point out that no similar studies have been found in the scientific literature with evidence showing this trend and difference between the 2 groups. In fact, the vast majority of studies refer to de novo patients as patients without a previous heart disease. Therefore, this study provides a different and novel point of view, which makes it particularly relevant.

In conclusions, patients who are hospitalized for the first time for decompensated HF without a previous diagnosis of HF have a higher long-term mortality than those who are already diagnosed with HF and experience a decompensation episode.

## Disclosures

The authors have no conflicts of interest to declare.

## References


1. Kurmani S, Squire I. Acute heart failure: definition, classification and epidemiology. *Curr Heart Fail Rep* 2017;14:385–392.
2. Xanthopoulos A, Butler J, Parissis J, Polyzogopoulou E, Skoularigis J, Triposkiadis F. Acutely decompensated versus acute heart failure: two different entities. *Heart Fail Rev* 2020;25:907–916.
3. Arrigo M, Parissis JT, Akiyama E, Mebazaa A. Understanding acute heart failure: pathophysiology and diagnosis. *Eur Heart J Suppl* 2016;18(suppl G):G11–G18.
4. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, B€ohm M, Burri H, Butler J, C~elutkiene_ J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [published correction appears in Eur Heart J. 2021 Oct 14;:]. *Eur Heart J* 2021;42:3599–3726.
5. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Gilard M, Haugaa KH, Jeppsson A, J€uni P, Pierard L, Prendergast BD, S'adaba JR, Tribouilloy C, Wojakowski W, ESC/ EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022;43:561–632.
6. Raffaello WM, Henrina J, Huang I, Lim MA, Suciadi LP, Siswanto BB, Pranata R. Clinical characteristics of de novo heart failure and acute decompensated chronic heart failure: are they distinctive pheno- types that contribute to different outcomes? *Card Fail Rev* 2021;7: e02.
7. Franco J, Formiga F, Chivite D, Manzano L, Carrera M, Ar'evalo-Lor- ido JC, Epelde F, Cerqueiro JM, Serrado A, Pérez-Barquero MM, RICA Investigadors. New onset heart failure−Clinical characteristics and short-term mortality. A RICA (Spanish registry of acute heart failure) study. *Eur J Intern Med* 2015;26:357–362.
8. Pranata R, Tondas AE, Yonas E, Vania R, Yamin M, Chandra A, Siswanto BB. Differences in clinical characteristics and outcome of de novo heart failure compared to acutely decompensated chronic heart failure - systematic review and meta-analysis. *Acta Cardiol* 2021;76:410–420.

9. Berkovitch A, Maor E, Sabbag A, Chernomordik F, Elis A, Arbel Y, Goldenberg I, Grossman E, Klempfner R. Precipitating factors for acute heart failure hospitalization and long-term survival. *Medicine (Baltimore)* 2015;94:e2330.
10. Gheorghiade M, Abraham WT, Albert NM, Greenberg BH, O'Connor CM, She L, Stough WG, Yancy CW, Young JB, Fonarow GC, OPTI- MIZE-HF Investigators and Coordinators. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospital- ized with acute heart failure. *JAMA* 2006;296:2217–2226.
11. Aguirre Tejedo A, Miró Ó. Prevalencia de factores precipitantes de insuficiencia cardiaca aguda y su impacto pronóstico: una revisión sistemática [Precipitating factors in acute heart failure: a review]. *Emergencias* 2017;29:185–193.
12. AlHabib KF, Kashour T, Elasfar AA, Alfaleh H, Hersi A, Alshamiri M, Alshaer F, Mimish L, Almasood A, AlHabeeb W, AlGhamdi S, Ghabashi A, Asfina K, Altaradi H, Alnobani O, Alkamel N, Thalib L. Long-term mortality rates in acute de novo versus acute-on-chronic heart failure: from the heart function assessment registry trial in Saudi Arabia. *Angiology* 2015;66:837–844.
13. Sinnenberg L, Givertz MM. Acute heart failure. *Trends Cardiovasc Med* 2020;30:104–112.
14. Sulaiman K, Panduranga P, Al-Zakwani I, Alsheikh-Ali AA, AlHabib KF, Al-Suwaidi J, Al-Mahmeed W, AlFaleh H, Elasfar A, Al-Motar- reb A, Ridha M, Bulbanat B, Al-Jarallah M, Bazargani N, Asaad N, Amin H. Clinical characteristics, management, and outcomes of acute heart failure patients: observations from the Gulf acute heart failure registry (Gulf CARE). *Eur J Heart Fail* 2015;17:374–384.
15. Hummel A, Empe K, D€orr M, Felix SB. De novo acute heart failure and acutely decompensated chronic heart failure. *Dtsch Arztebl Int* 2015;112:298–310.
16. Anker SD, Doehner W, Rauchhaus M, Sharma R, Francis D, Knosalla C, Davos CH, Cicoira M, Shamim W, Kemp M, Segal R, Osterziel KJ, Leyva F, Hetzer R, Ponikowski P, Coats AJ. Uric acid and survival in chronic heart failure: validation and application in metabolic, func- tional, and hemodynamic staging. *Circulation* 2003;107:1991–1997.
17. López-Vilella R, Marqués-Sulé E, Sánchez-Lázaro I, Laymito Quispe R, Martínez Dolz L, Almenar Bonet L. Creatinine and NT-ProBNP levels could predict the length of hospital stay of patients with decom- pensated heart failure. *Acta Cardiol* 2021;76:1100–1107.

18. Brouwers FP, de Boer RA, van der Harst P, Voors AA, Gansevoort RT, Bakker SJ, Hillege HL, van Veldhuisen DJ, van Gilst WH. Inci- dence and epidemiology of new onset heart failure with preserved vs. reduced ejection fraction in a community-based cohort: 11-year fol- low-up of PREVEND. *Eur Heart J* 2013;34:1424–1431.
19. Younis A, Mulla W, Goldkorn R, Klempfner R, Peled Y, Arad M, Freimark D, Goldenberg I. Differences in mortality of new-onset (de- novo) acute heart failure versus acute decompensated chronic heart failure. *Am J Cardiol* 2019;124:554–559.
20. Franco J, Formiga F, Corbella X, Conde-Martel A, Llácer P, Álvarez Rocha P, Ormaechea Gorricho G, Satué J, Soler Rangel L, Manzano L, Montero-Pérez-Barquero M, en nombre del Grupo de investigadores RICA; Miembros del registro RICA. De novo acute heart failure: clinical features and one-year mortality in the Spanish nationwide Registry of Acute Heart Failure. *Med Clin (Barc)* 2019; 152:127–134.
21. Choi KH, Lee GY, Choi JO, Jeon ES, Lee HY, Cho HJ, Lee SE, Kim MS, Kim JJ, Hwang KK, Chae SC, Baek SH, Kang SM, Choi DJ, Yoo BS, Kim KH, Park HY, Cho MC, Oh BH. Outcomes of de novo and acute decompensated heart failure patients according to ejection fraction. *Heart* 2018;104:525–532.
22. Lassus JP, Siiril€a-Waris K, Nieminen MS, Tolonen J, Tarvasm€aki T, Peuhkurinen K, Melin J, Pulkki K, Harjola VP, FINN-AKVA study group. Long-term survival after hospitalization for acute heart failure −differences in prognosis of acutely decompensated chronic and new- onset acute heart failure. *Int J Cardiol* 2013;168:458–462.
23. Senni M, Gavazzi A, Oliva F, Mortara A, Urso R, Pozzoli M, Metra M, Lucci D, Gonzini L, Cirrincione V, Montagna L, Di Lenarda A, Maggioni AP, Tavazzi L, IN HF Outcome Investigators. In-hospital and 1-year outcomes of acute heart failure patients according to presentation (de novo vs. worsening) and ejection fraction. Results from IN-HF outcome registry. *Int J Cardiol* 2014;173:163–169.
24. García-Gutiérrez S, Antón-Ladislao A, Quiros R, Lara A, Rilo I, Moril- las M, Murga N, Gallardo MS, Lafuente I, Aguirre U, Quintana JM, ESSIC −REDISSEC Group. Short-term mortality risk score for de novo acute heart failure (ESSIC-FEHF). *Eur J Intern Med* 2020;77:52–58.
25. Moliner P, Comin-Colet J. First episode of acute heart failure: can we already predict the risk of short-term mortality? *Eur J Intern Med* 2020;77:30–31.
26. Borovac JA, Glavas D, Bozic J, Novak K. Predicting the 1-year all-cause mortality after hospitalisation for an acute heart failure event: a real-world derivation cohort for the development of the $S_2$PLiT-UG score. *Heart Lung Circ* 2020;29:687–695.

27. Greene SJ, Hernandez AF, Dunning A, Ambrosy AP, Armstrong PW, Butler J, Cerbin LP, Coles A, Ezekowitz JA, Metra M, Starling RC, Teerlink JR, Voors AA, O'Connor CM, Mentz RJ. Hospitalization for recently diagnosed versus worsening chronic heart failure: From the ASCEND-HF Trial. *J Am Coll Cardiol* 2017;69:3029–3039.
28. Degoricija V, Trbusi'c M, Potocnjak I, Radulovi'c B, Teresak SD, Pregartner G, Berghold A, Tiran B, Frank S. Acute Heart Failure developed as worsening of Chronic Heart Failure is associated with increased mortality compared to de novo cases [published correction appears in *Sci Rep* 2019;9:8403]. *Sci Rep* 2018; 8:9587.
29. Parenica J, Spinar J, Vitovec J, Widimsky P, Linhart A, Fedorco M, Vaclavik J, Miklik R, Felsoci M, Horakova K, Cihalik C, Malek F, Spinarova L, Belohlavek J, Kettner J, Zeman K, Dusek L, Jarkovsky J, AHEAD Main investigators. Long-term survival following acute heart failure: the Acute Heart Failure Database Main registry (AHEAD Main). *Eur J Intern Med* 2013;24:151–160.
30. Investigators SOLVD, Yusuf S, Pitt B, Davis CE, Hood WB Jr, Cohn JN. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions [published correction appears in *N Engl J Med* 1992;327:1768]. *N Engl J Med* 1992;327:685–691.

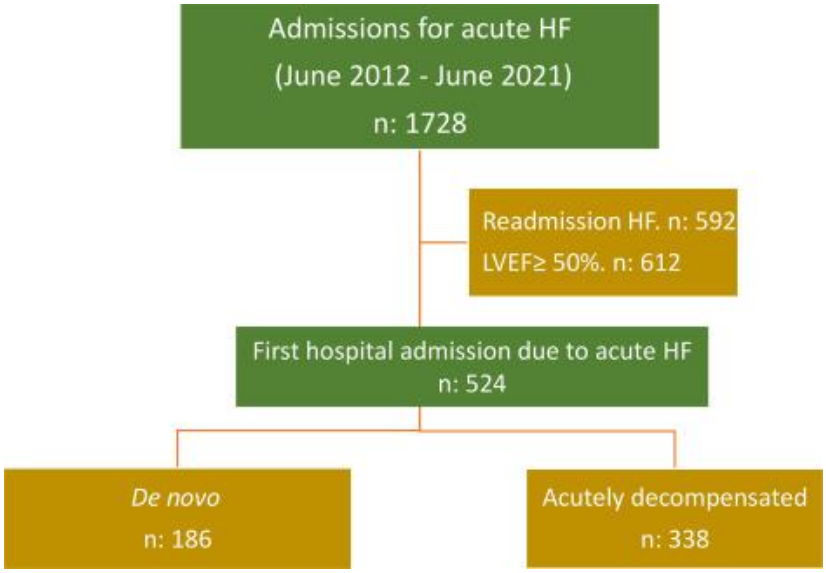



**Figure 1**. Flow chart of patient selection.

**Table 1**. Clinical profile of patients

| | First admission for decompensated HF "*de novo*" (n) 186 | First admission for decompensated HF "*acutely decompensated*" (n) 338 | Statistical significance |
|---|---|---|---|
| Sex male (n,%) | 111 (59.7) | 192 (56.8) | 0.293 |
| Age (years)* | 73.6±13.9 | 73.8±12.9 | 0.872 |
| Baseline heart disease (n,%)† | | | |
| Hypertensive | 43 (23.2) | 90 (26.6) | 0.377 |
| Ischemic | 53 (28.5) | 85 (25.1) | 0.405 |
| DCMi | 21 (11.3) | 44 (13.0) | 0.566 |
| Valvular | 40 (21.5) | 91 (26.9) | 0.171 |
| Other | 29 (15.3) | 28 (8.3) | 0.01 |
| History (n,%) | | | |
| Previous cardiac surgery | 25 (13.4) | 76 (22.5) | 0.012 |
| Hypertension | 148 (79.6) | 279 (82.5) | 0.402 |
| Dyslipidemia | 104 (55.9) | 193 (57.1) | 0.793 |
| Diabetes Mellitus | 82 (44.1) | 139 (41.1) | 0.511 |
| Smoking | 73 (39.2) | 128 (37.9) | 0.756 |
| Alcoholism | 16 (8.6) | 18 (5.3) | 0.145 |
| COPD | 25 (13.4) | 41 (12.1) | 0.665 |
| Sleep apnea syndrome | 20 (10.8) | 40 (11.8) | 0.710 |
| Obesity | 42 (22.6) | 51 (15.1) | 0.032 |
| Renal dysfunction | 44 (23.7) | 93 (27.5) | 0.336 |
| Hypothyroidism | 8 (4.3) | 41 (12.1) | 0.003 |
| AF/atrial flutter | 86 (46.2) | 208 (61.5) | 0.001 |
| Stroke | 29 (15.6) | 33 (9.8) | 0.048 |
| Peripheral vascular disease | 14 (7.5) | 19 (5.6) | 0.390 |
| Peritoneal dialysis | 2 (1.1) | 0 (0.0) | 0.242 |
| Cause of decompensation (n,%) | | | |
| Arrhythmic | 56 (30.1) | 47 (13.9) | 0.0001 |
| Hypertension | 52 (28.0) | 51 (15.1) | 0.0001 |

**Table 1**. Clinical profile of patients

| | First admission for decompensated HF "*de novo*" (n) 186 | First admission for decompensated HF "*acutely decompensated*" (n) 338 | Statistical significance |
|---|---|---|---|
| Infectious | 45 (24.2) | 78 (23.1) | 0.773 |
| Ischemic | 15 (8.1) | 115 (34.0) | 0.0001 |
| Unknown/other | 18 (9.6) | 47 (13.9) | 0.160 |
| Hemodynamic pattern (n,%) | | | |
| Pulmonary congestion | 149 (80.1) | 267 (79.0) | 0.763 |
| Systemic congestion | 18 (9.7) | 43 (12.7) | 0.298 |
| Pulmonary/systemic congestion | 16 (8.6) | 9 (2.7) | 0.002 |
| Low output | 3 (1.6) | 19 (5.6) | 0.050 |
| Height (cm)* | 164.8±8.7 | 162.8±9.0 | 0.132 |
| Weight (kg)* | 80.4±18.6 | 74.5±17.9 | 0.001 |
| SBP at admission* | 144.5±29.1 | 139.0±29.0 | 0.036 |
| DBP at admission* | 82.1±19.5 | 78.3±17.1 | 0.02 |
| HR at admission* | 95.0±27.2 | 85.6±22.1 | 0.0001 |
| HF nursing program (n,%) | 0 (0.0) | 12 (3.6) | 0.022 |
| Included in clinical trial (n,%) | 0 (0.0) | 11 (3.3) | 0.009 |

∗ Mean and standard deviation.

† Baseline heart disease refers to the etiology of HF in patients.

AF = Atrial fibrillation; COPD = Chronic Obstructive Pulmonary Disease; DBT = diastolic blood pressure; DCMi = Idiopathic dilated cardiomyopathy; HF = Heart failure; HR = Heart rate; SBP = Systolic blood pressure.

**Table 2**. Electrocardiographic, echocardiographic and analytical characteristics

| | First admission for decompensated HF "*de novo*" (n) 186 | First admission for decompensated HF "*acutely decompensated*" (n) 338 | Statistical significance |
|---|---|---|---|
| Rhythm on admission (n,%) | | | |
| AF/atrial flutter | 102 (54.8) | 148 (43.8) | 0.015 |
| Sinus | 75 (40.3) | 143 (42.3) | 0.659 |
| Pacemaker | 7 (3.8) | 40 (11.8) | 0.002 |
| Other rhythms | 2 (1.1) | 7 (2.1) | 0.625 |
| LVEF (n,%) | | | |
| Mild depression | 17 (9.1) | 34 (10.1) | 0.734 |
| Moderate depression | 58 (31.2) | 88 (26.0) | 0.209 |
| Severe depression | 111 (59.7) | 216 (63.9) | 0.339 |
| Dilated LV (n,%) | 54 (29.0) | 105 (31.1) | 0.628 |
| Severe MR (n,%) | 22 (11.8) | 44 (13.0) | 0.694 |
| Severe MS (n,%) | 1 (0.5) | 8 (2.4) | 0.234 |
| Severe AS (n,%) | 24 (12.9) | 27 (8.0) | 0.069 |
| Severe AR (n,%) | 4 (2.2) | 7 (2.1) | 0.797 |
| Severe TR (n,%) | 17 (9.1) | 71 (21.0) | 0.001 |
| Dilated LA (n,%) | 149 (80.1) | 250 (74.0) | 0.114 |
| LV hypertrophy (n,%) | 91 (48.9) | 166 (49.1) | 0.967 |
| RV function(n,%) | | | |
| Normal | 149 (80.1) | 233 (68.9) | 0.006 |
| Mild depression | 11 (5.9) | 34 (10.1) | 0.105 |
| Moderate depression | 13 (7.0) | 44 (13.0) | 0.034 |
| Severe depression | 13 (7.0) | 27 (8.0) | 0.680 |
| Dilated RV (n,%) | 41 (22.0) | 88 (26.0) | 0.310 |
| Admission blood test* | | | |
| Urea | 43.0 (27) | 54.5 (35) | 0.0001 |
| Creatinine | 1.1 (0.62) | 1.0 (0.53) | 0.223 |
| Glomerular filtration rate | 60.0 (34.5) | 47.5 (21.0) | 0.391 |
| Total bilirubin | 0.62 (0.78) | 0.67 (0.62) | 0.665 |
| ASAT-GOT | 20.0 (25.0) | 23.5 (24.5) | 0.293 |
| ALAT-GPT | 20.0 (18.0) | 22.0 (17.0) | 0.768 |
| TnTu | 29.0 (38.4) | 54.1 (72.18) | 0.306 |

**Table 2**. Electrocardiographic, echocardiographic and analytical characteristics

| | First admission for decompensated HF "*de novo*" (n) 186 | First admission for decompensated HF "*acutely decompensated*" (n) 338 | Statistical significance |
|---|---|---|---|
| NT-ProBNP | 2,846.0 (4,872.0) | 3,694.5 (9,229.5) | 0.098 |
| Sodium | 140.0 (6.0) | 141.0 (4.0) | 0.060 |
| Potassium | 4.3 (0.7) | 4.3 (0.7) | 0.374 |
| Hemoglobin | 12.6 (2.9) | 12.6 (2.5) | 0.252 |
| Hematocrit | 38.4 (8.5) | 38.5 (7.5) | 0.717 |
| Uric acid | 7.2 (2.4) | 8.3 (3.3) | 0.0001 |
| Transferrin saturation index | 16.0 (12.0) | 16.0 (9.0) | 0.817 |
| Ferritin | 116.0 (175.8) | 154.5 (188.8) | 0.374 |
| CA125 | 76.5 (129.1) | 76.4 (146.9) | 0.814 |

∗ Median and interquartile range.

AF = Atrial fibrillation; ALAT-GPT = Alanine aminotransferase; AR = Aortic regurgitation; AS = Aortic stenosis; ASAT-GOT = Aspartate aminotransferase; CA125 = Carboxyembryonic antigen 125; LA = Left atrium; LV = Left ventricle; LVEF = Left ventricular ejection fraction; MR = Mitral regurgitation; MS = Mitral stenosis; NT-ProBNP = N-terminal pro-brain natriuretic peptide; RV = right ventricle; RVEF = Right ventricular ejection fraction; TnTu = Troponin T ultrasensitive; TR = Tricuspid regurgitation.

**Table 3**. Pre-admission treatments

| | First admission for decompensated HF "*de novo*" (n) 186 | First admission for decompensated HF "*acutely decompensated*" (n) 338 | Statistical significance |
|---|---|---|---|
| ACEI/ARB II (n,%) | 108 (58.1) | 213 (63.0) | 0.370 |
| INRA (n,%) | 5 (5.8) | 81 (24.0) | 0.0001 |
| βblockers (n,%) | 75 (40.3) | 216 (63.9) | 0.0001 |
| MRA (n,%) | 25 (13.4) | 307 (90.8) | 0.0001 |
| Ivabradine (n,%) | 25 (13.4) | 74 (21.9) | 0.018 |
| Loop diuretic (n,%) | 15 (8.1) | 321 (95.0) | 0.0001 |
| Thiazides (n,%) | 15 (8.1) | 30 (8.9) | 0.751 |
| Tolvaptan (n,%) | 0 (0.0) | 4 (1.2) | 0.335 |
| Acetazolamide (n,%) | 0 (0.0) | 7 (2.1) | 0.114 |
| SGLT2i(n,%) | 43 (23.1) | 104 (30.8) | 0.078 |
| Nitrates (n,%) | 22 (25.6) | 6 (1.8) | 0.0001 |
| Digoxin (n,%) | 3 (1.6) | 50 (14.8) | 0.0001 |
| Antiarrhythmics (n,%) | 19 (4.8) | 88 (26.0) | 0.0001 |
| Statins (n,%) | 93 (50.0) | 149 (44.1) | 0.194 |
| Calcium antagonists (n,%) | 84 (45.2) | 13 (3.8) | 0.0001 |
| Allopurinol (n,%) | 24 (12.9) | 162 (47.9) | 0.0001 |
| Pulmonary vasodilators (n,%) | 1 (0.5) | 14 (4.1) | 0.036 |

ACE inhibitors/ARII = angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonists; ARM = mineralocorticoid receptor antagonists; ARNI = angiotensin receptor and neprilysin inhibitor; HF = heart failure; iSGLT2 = sodium-glucose cotransporter type 2 inhibitors.

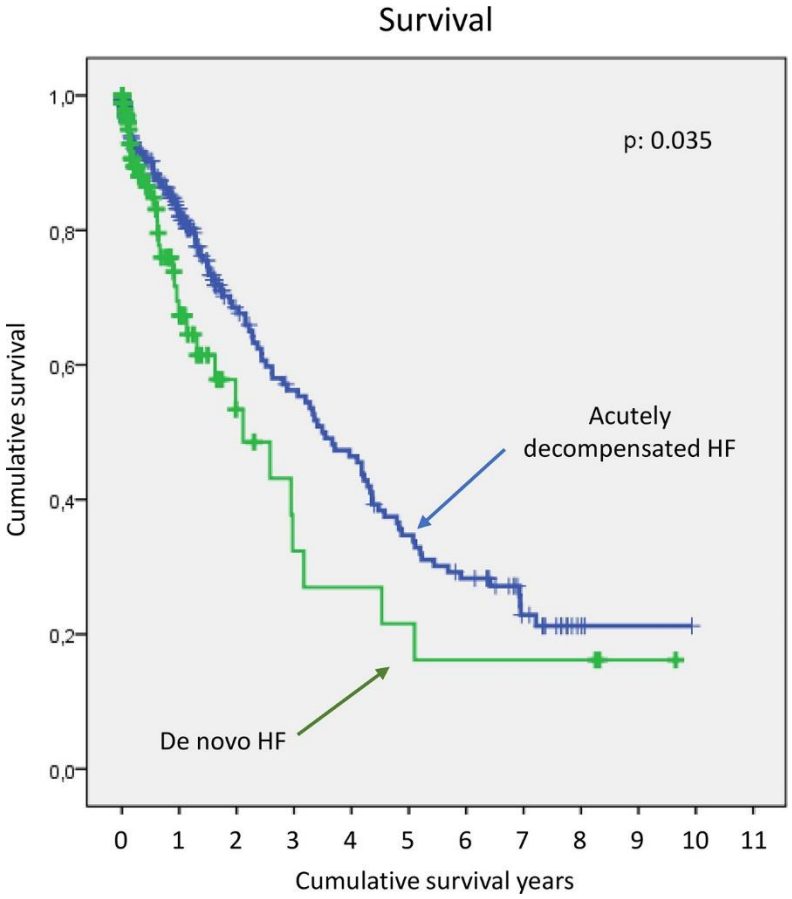



**Figure 2**. Survival function.

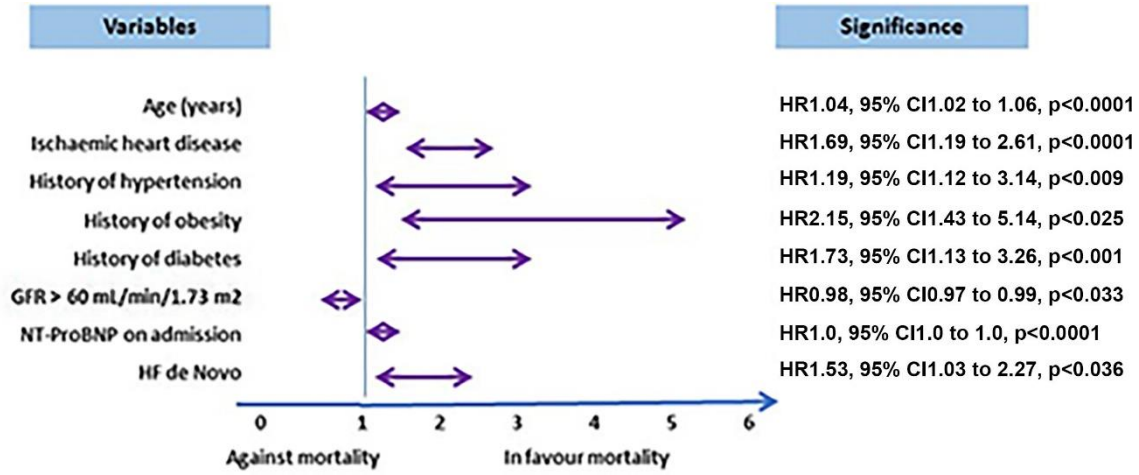



**Figure 3**. Multivariate mortality analysis. DM = diabetes mellitus; GFR = glomerular filtration rate.