

Editorial

Mortality and Heart Failure Hospitalizations. The Need for an Exhaustive, Official, and Standardized Registry



Mortalidad y reingresos por insuficiencia cardiaca: la necesidad de un registro oficial completo, abierto y homologable

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“The only source of knowledge is experience”
A. Einstein

Access to reliable data on a specific disease can help to better understand the condition and its effect patients' lives, and to seek improvements in its management.

Recently, *Revista Española de Cardiología* published an interesting article by Martínez Santos et al.¹ on in-hospital mortality related to heart failure (HF), and on readmissions and mortality at 30 days and 1 year. This study provides data worth highlighting and points out issues remaining to be resolved.

The first point to consider before discussing the article is that the number of HF-related hospitalizations has continued to increase in Spain in the last 5 years, but perhaps not as intensely as in previous periods. According to the National Institute of Statistics, there were 79 970 HF-related discharges in Spain in 2003 (the first year data on this diagnosis were published), 96 820 in 2007 (representing a 21% increase in 4 years), 114 576 in 2012 (18% increase in 5 years), and 127 714 in 2017 (11% in 5 years).² Perhaps the establishment of HF programs and dedicated units over these last years^{3,4} has kept this rate lower than would be expected considering the aging of the population and the greater progression to chronicity of acute heart diseases.

In 2012 more than 86 000 hospital discharges were documented in the national health system, and 77 652 of them were analyzed by Martínez Santos et al.¹; that is, 68% of hospitalizations documented by the National Institute of Statistics. Therefore, we have a broad picture of what occurs in HF patients in our country, but it is not complete.

Of note, the in-hospital mortality rate (9.2%) does not seem to have varied significantly with respect to values in earlier studies. Although the data come from different sources and are more local, the reported mortality rates in Spain range from 6.4% in the study by Permanyer et al. (2002) in patients of all ages hospitalized in any department⁵ to 11% in the study by Formiga et al. (2007) in geriatric patients,⁶ and they include a rate of 9.5% in the study by

Hermida et al. (2008) in patients hospitalized in an internal medicine department.⁷ It is likely that beyond the therapy “failures” seen in recent clinical trials in acute HF,⁸ patients' increasingly greater comorbidity plays an important role in this lack of a significant reduction in mortality in the acute phase. This parameter may also have improved somewhat since the study by Martínez Santos et al.¹ For example, in Germans Trias i Pujol Hospital in Badalona, mortality declined discretely and slowly, but in a progressive manner from 2012 (9.4%) to 2018 (8%; $P = .003$). In the European Society of Cardiology Heart Failure Long-Term registry (ESC-HF-LT), an analysis of 5039 HF patients hospitalized between 2011 and 2013 found a 4.9% rate of in-hospital deaths,⁹ a value much lower than that reported by Martínez Santos et al., but the patients included were considerably younger (69 years on average) and probably had fewer comorbidities.

Of particular interest, no significant relationship was found between the technical resources used in this condition (hemodynamic procedures, cardiac surgery, and heart transplant) and mortality, at least independently of the volume of admissions. This finding is understandable because these resources are used in only a small percentage of the total number of patients hospitalized for HF, and in many cases mortality is related more to the comorbidities than the heart condition, itself (remember, mean age was 79 years). In contrast, there was an association with the availability of a structured cardiology department, although we do not know whether this relationship was independent of the volume of admissions. Given that a large percentage of patients are admitted for HF in hospital departments other than cardiology, it is plausible that when a hospital has a dedicated cardiology department, it would also have other infrastructures inherent to this type of hospital: an integrated HF unit or program, a day hospital equipped to administer intravenous diuretics, specialized interconsultations, and other factors that could favor the lower mortality observed as well as the high volume of HF admissions, as the authors mention in the discussion of their article.

The article does not explicitly state the 1-year HF readmission rate, but it can be extrapolated from the data provided. It was around 20%, a value similar to the 18.7% reported in the ESC-HF-LT registry. The previous pilot study (ESC-HF pilot)¹⁰ had cited an HF readmission rate of 24.8%, but the data were from an earlier period (2009–2010). Although these values show that the results in our health system are consistent with the European mean, it may be possible to improve the number of readmissions at 30 days and

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1 year through specific structured care, as seen in later years in more limited studies.^{11,12} In the UMIPIC¹³ program, the 1-year HF readmission rate was 35%, but the population studied had a particularly high risk of rehospitalization. When the rate in the year prior to inclusion in the program was compared to that of the year after inclusion in the same patient cohort, an 85% reduction in the number of HF admissions was actually achieved. These findings support the notion that both morbidity and mortality in this disease largely depend on the patients' comorbidities, and that better knowledge of these factors can lead to better outcomes, regardless of the possible future improvements in cardiologic treatment of HF. Hence, the importance of having reliable registry data: the more complete and trustworthy, the better.

The article by Martínez Santos et al.¹ also shows predictive models of death and rehospitalization, with the limitation expressed by the authors (discussed later) that out-of-hospital deaths could not be included as a competing risk with the risk of rehospitalization, as this information was not available. Historically, it has always been more difficult to estimate the risk of hospital admittance due to HF than the risk of death.¹⁴ The criteria used as a basis for the decision to admit a patient vary considerably and are determined by the existing infrastructure and outpatient care programs, which may or may not include day hospitals or "hot" clinics where, for example, intravenous diuretics can be administered. In the study discussed here, the area under the curve (AUC) for 30-day mortality was 0.715 in the logistic regression model and 0.735 in the multilevel model, which decreased to 0.684 and 0.706, respectively, for (in-hospital) mortality at 1 year. Although the specific variables entered in the model were not described, it is assumed that they were those found to be significant in the multivariate analysis. Nor did the authors specify whether the time to event was taken into account in the 1-year model (Somers' dxy rank correlation). This always results in somewhat lower AUCs than those obtained by logistic regression, which consider the event in a dichotomous manner.¹⁵ As would be expected, the AUCs for predicting rehospitalization (in this case for a cardiovascular cause and without competing risks) were somewhat lower (0.598 at 30 days and 0.612 at 1 year).

The variables used in the related predictive models vary considerably and are based on different definitions. Some models tend to reduce the variables to a minimum (eg, by performing a backward stepwise multivariate analysis, as was done in the study in question), whereas others include a large number of variables. Apart from clinical and sociodemographic variables, some studies have evaluated systematic analytical determinations and various biomarkers,^{16,17} which, in some cases have improved the predictive capacity of the model. For example, the recent BIostat-CHF¹⁶ study, performed in a mixed population of hospitalized and outpatients, developed predictive models including the biomarker NT-proBNP and obtained an AUC of 0.73 for all-cause mortality and 0.69 for HF hospitalization using a competing risks method. Our group analyzed several biomarkers in addition to clinical variables in a very elderly patient cohort discharged after an index admission for HF.¹⁷ We obtained a C statistic of 0.750 for 30-day all-cause death or hospitalization with a model that included age, sex, diabetes, urea, Charlson Comorbidity Index, and Barthel Index, together with ST2 and NT-proBNP. For the same composite endpoint at 1 year, the C statistic was 0.780 with a model that included age, sex, New York Heart Association functional class, hemoglobin, Charlson Comorbidity Index, Barthel Index, ST2, and NT-proBNP. Finally, the C statistic was 0.786 for 1-year all-cause death with a model that included the same clinical variables, but incorporated the biomarkers ST2 and CA125. Obviously, all the predictive models used cannot be compared, as the variables included and patient populations differ between them. Although in a different context, the MEESSI¹⁸ scale was recently validated with

good results in 30 hospital emergency departments in Spain. The scale obtained a C statistic for 30-day all-cause death of 0.81 for the model with "imputed data" (4711 patients) and 0.753 for the model with "observed data" (602 patients). This scale includes 13 variables, among them NT-proBNP and troponin values.

Finally, some thoughts about our registries. The study by Martínez Santos et al. was based on the Minimum Data Set (CMBD; *Conjunto Mínimo Básico de Datos*) compiled in the Spanish national health system, and it provides a snapshot of the results in Spain. The reliability of the CMBD data may be debatable and likely varies depending on the time period and region of the country reviewed. The factors influencing the quality of the data obtained through the CMBD have been fully described and perfectly analyzed,¹⁹ and it is not our intention to delve into these limitations; nonetheless, it is important to be aware of them. Irrespective of this consideration, the information undoubtedly enables only a partial analysis of the disease. The current nationwide registries of data on hospitalization, treatment, and outcomes of various diseases are likely far from the large, complete and reliable registries that have been in use for some time now in certain Nordic countries. One of these is the Danish National Patient Registry, which, with a single 10-digit identifier number common to all, can be linked to the Registry of Medicinal Product Statistics and the Registry of Causes of Death. These comprehensive registries should serve as an inspiration for efforts in Spain. We believe that it is essential to create an official Spanish Heart Failure Registry that is comparable to those functioning in the north of Europe and make it available to all researchers.

In our modest opinion, an important limitation of the article by Martínez Santos et al. is the absence of information on out-of-hospital deaths. The authors recognize this limitation, but tend to minimize it in their discussion, mentioning that proportionately few hospitalized HF patients die outside the hospital in the year following admittance; that is, outside of a rehospitalization. In our study, including patients attended in a dedicated center after discharge for HF,¹² only 56% of deaths that occurred during the following year were in a rehospitalization; 28% occurred at home and 16% in a social-health center after transfer from the index admission. Therefore, the true 1-year mortality may have been significantly higher than the value derived from an analysis of the CMBD. Exclusion of these out-of-hospital deaths was further justified by noting that the Ministry of Health and Consumer Affairs only provides information on hospital discharges. However, Spain also has the National Death Index (INDEF, *Índice Nacional de Defunciones*), which is also dependent on the Ministry of Health and Consumer Affairs.

The INDEF is an information system created by order of the Ministry of the Presidency (Order of 25 February, 2000, by which the National Death Index is created and regulated), and it contains the personal data of each death recorded in civil registries throughout the country. The INDEF has a database structure and data have been entered since 1987. It is developed from the data files provided by the Ministries of Justice, of Economy, and of Finance to the Ministry of Health, Social Services, and Equality through the National Institute of Statistics. Specifically, the Subdirector General of Health Information and Evaluation (formerly the Health Information Institute) of the Directorate General of Public Health, Quality, and Innovation is in charge of developing and managing the Index for the purposes intended. It should be noted that the Index contains no information regarding the cause of death.²⁰

Therefore, in the current technological era, it should not be an insurmountable task to cross identify and obtain complete data on patient outcomes. In addition to yielding imprecise information on total mortality, the lack of information on out-of-hospital deaths meant that the rehospitalization rate could not be analyzed with competing risks

As a final message, the article by Martínez Santos et al. presents a general view of the number of patients hospitalized for HF in Spain in 2012 and their short- and long-term outcomes, and provides acceptable data on morbidity and mortality, above all taking into account the patients' age and comorbidity. Administrative bodies should take measures to facilitate juxtaposition of information from the various existing registries, including data on pharmaceutical use and consumption of other resources, so that more complete and accurate analyses can be carried out that will help improve the management and treatment of our patients.

CONFLICTS OF INTEREST

None declared.

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