Precipitating factors of heart failure admission: Differences related to age and left ventricular ejection fraction

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ABSTRACT

Aim: To evaluate precipitating factors (PF) of exacerbation in heart failure (HF) and their relationship with age, preserved vs. reduced left ventricular ejection fraction (LVEF) and short-term prognosis.

Methods: We included and followed 2962 patients admitted with acute HF to Internal Medicine Units. Several PF were identified. Differences in PF according to preserved vs. reduced LVEF and age (patients ≥ 80 years vs. younger) were analyzed. Primary endpoints were readmission due to worsening HF and all-cause mortality at 3 months follow-up. Multivariable Cox models were conducted to identify the independent predictors of 3-months mortality and readmission.

Results: More than half of the patients were 80 years and over, 47% were women and 61% had preserved LVEF. Atrial fibrillation (AF) and myocardial ischemia were the more common cause of decompensation among octogenarians. It was more frequent to find myocardial ischemia or non-adherence to treatment as precipitants in patients with systolic dysfunction. However, respiratory infections, AF and poor control of blood pressure were more usual in patients with preserved LVEF compared to those with LVEF <50%.

Patients admitted for HF precipitated by myocardial ischemia had a higher risk of readmission at 3 months (HR 1.49; CI 95%: 1.12–1.99, p = 0.006) and the longest hospital stay (12 days). PF showed no predictive value for mortality.

Conclusion: Myocardial ischemia as a PF was an independent marker for HF readmissions at 3-months follow-up. Precipitants are different depending on the age and LVEF of patients. Their identification could improve risk stratification and prevention strategies.

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1. Introduction

Hospitalization for heart failure (HF) continues to increase despite advances in treatment. Most hospital admissions occur in people aged 65 or older [1].

Acute HF, either new onset or exacerbation, is precipitated by several conditions or diseases. Precipitating factors (PF) of decompensation in patients with HF may be cardiac (such as uncontrolled hypertension, arrhythmia or ischemia) or extra-cardiac (medication or dietary non-compliance, infections…). The extra-cardiac precipitants are the most common and have particular relevance for elderly [2,3]. However, there is only limited information on the prevalence and role as PF in this population.

Identifying potential PF of exacerbation and knowing their impact on the hospital length of stay (LOS) and the prognosis of these patients could be of interest to avoid future relapses. Moreover, the identification of predictors of readmission in especially vulnerable population subgroups, such as the elderly, may provide useful insight for clinicians in designing prevention strategies. Although some studies have explored the factors leading to decompensation, they have mostly

been conducted with younger patients [4–8] or mainly in systolic dis-function [7,9–10]. Therefore, information is lacking in relation to PF in very elderly and preserved LVEF HF patients, the group with the highest number of readmissions. Furthermore, the evaluation of a possible prognostic effect of PF has been barely assessed [2–3,11–12]. There are only a few prospective papers [13–14], most of them evaluating only in-hospital mortality.

The objective of this study was to prospectively describe the PF associated with exacerbations of HF, exploring possible differences according to the age and LVEF, and to evaluate their influence on short-term (3-months) prognosis after discharge.

2. Methods

2.1. Population

This study includes a prospective, longitudinal, multicenter cohort of patients with HF admitted to Internal Medicine Units of 52 Spanish hospitals from February 2008 to November 2014. The Spanish National Registry on Heart Failure (RICA) is supported by the Heart Failure Working Group of the Spanish Society of Internal Medicine. This nationwide registry includes participants of both sexes, aged 50 and older, with HF according to the criteria of the European Society of Cardiology [15]. The RICA registry has been described in previous publications [16,17].

Exclusion criteria for our study were: a) HF due to pulmonary hypertension, b) death during index hospitalization and c) inability to participate.

2.2. Variables and blood sampling

Data were collected using a specifically designed web form (www. registrorica.org) [18].

Demographic and anthropometric data, medical history, cardiovascular risk factors and prevalent comorbidities were collected. Drugs prescribed at discharge, functional class in last month before admission (New York Heart Association, NYHA), LOS and LVEF determined by 2D echocardiography were also included. According to ESC Guidelines [15], preserved ejection fraction was defined as a LVEF equal to or greater than 50%.

Within the first 48 h of admission, blood samples were obtained to measure serum levels of hemoglobin, urea, creatinine, sodium, potassium, cholesterol, N-terminal pro B-type natriuretic peptide (NT-proBNP) and C reactive protein.

The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation (MDRD-4). Renal failure was defined as eGFR < 60 mL/min/1.73 m^2.

We collected all PF included in the RICA registry: respiratory infection, AF, non-adherence to treatment, uncontrolled hypertension, myocardial ischemia and others. Because of the "anemia" had not been collected as a proper FP, some patients in the group "others" were recoded. Thus, patients with hemoglobin below 9 g/dl without other PF of decompensation were included in a new independent group.

2.3. Ethics

The investigation conformed to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethical Committee of the University Hospital "Reina Sofía" (Córdoba, Spain). All patients signed informed consent at inclusion.

2.4. Endpoints

Primary end-points were readmission due to worsening HF and all-cause mortality at 3 months follow-up. Secondary end-point examined the association of PF with LOS.

2.5. Statistical analysis

A descriptive analysis of the sample was conducted. Continuous variables were tested for a normal distribution with the Kolmogorov–Smirnov test. Normally distributed data are presented as mean SD and non-normally distributed data as median with interquartile range.

Population was categorized into two groups according to age (<80 or ≥80 years) and LVEF (≥50% or <50%). Baseline differences between groups were contrasted by Chi-square test or by the Fisher's exact test for categorical variables. For continuous variables the Student's T test and the Kruskal–Wallis test were used to compare normal and non-normal variables, respectively. Univariate analysis to evaluate hazard ratios (HR) was performed using Cox proportional hazards models. Using the Cox regression model adjusted for variables with a p-value of 0.05 in the univariate analysis, a multivariate analysis was conducted to identify the independent predictors of 3-month mortality and readmission.

A p-value of less than 0.05 was considered statistically significant. For statistical analysis we used SPSS (version 18.0; SPSS Inc. Chicago. IL, USA) for Windows software.

3. Results

3.1. Baseline characteristics

A total of 2962 patients were included and followed for 3 months. Baseline characteristics of the total cohort and according to the groups of age are presented in Table 1.

Over half of the patients were over 80 years (53.4%) and 47% were women. Most patients were in a basal functional class NYHA II. Concerning comorbidity, hypertension was present in 85% of patients. Diabetes mellitus (46%) and chronic kidney disease (40%) were also very prevalent in our population. A significant proportion of patients had preserved LVEF (61%). The most common PF was respiratory infection (29%). Others frequently identified factors were AF (19%), lack of adherence to the treatment (6.3%), myocardial ischemia (6.3%), uncontrolled hypertension (6%) and anemia (3.4%). Of note was the large proportion of patients included in the group "others" (30%), that encompassed a number of minority PF.

3.2. Differences according to age (Table 1)

The group with older patients had a greater proportion of women, hypertensive etiology, worse renal function, more advanced functional class and higher levels of NT-proBNP. With regard to PF, AF (17 vs 22%, p = 0.002) and myocardial ischemia (5.4 vs 7.1%, p = 0.056) were more common causes of decompensation in older patients, and non-adherence to treatment in younger patients (8 vs 4.1, p < 0.001).

3.3. Differences according to LVEF

As summarized in Table 2, there were significant differences between groups according to LVEF. Thus, it was more common to find myocardial ischemia (3.8 vs. 10%, p < 0.01) or non-adherence to treatment (5.4 vs. 7.7%, p < 0.010) as precipitating factors in patients with LVEF < 50%. However, AF (21 vs. 17%, p = 0.002), poor control of blood pressure (6.7 vs. 4.9%, p = 0.041) and respiratory infections (31 vs. 25%, p < 0.001) were more frequent in patients with preserved LVEF compared to those with systolic dysfunction.

3.4. Length of stay

LOS, shown in Fig. 1, had differences up to 4 days depending on PF of admission (p < 0.001). Thus, patients decompensated by uncontrolled hypertension had the shortest LOS and were hospitalized for less than