



## Original article

## Influence of atrial fibrillation on the mortality of patients with heart failure with preserved ejection fraction<sup>☆</sup>

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## ABSTRACT

**Introduction and objectives:** The impact of atrial fibrillation (AF) on the prognosis of heart failure with preserved ejection fraction (HFpEF) is still the subject of debate. We analysed the influence of AF on the prognosis on mortality and readmission in patients with HFpEF.

**Methods:** Prospective observational study in 1971 patients with HFpEF, who were admitted for acute heart failure. Patients were divided into 2 groups according to the presence or absence of AF. We analysed mortality, readmissions and combined mortality/readmissions at one-year follow-up.

**Results:** A total of 1177 (59%) patients had AF, mean age 80.3 (7.8) years and 1233 (63%) were women. Patients with HFpEF and AF were older, female, greater valvular aetiology and lower comorbidity measured by the Charlson index. At the one-year follow-up, 430 (22%) patients had died and 840 (43%) had been readmitted. In the 2 groups analysed, there was no difference in all-cause mortality (22 vs. 21%;  $p = 0.739$ , AF vs. no-AF, respectively) or cardiovascular causes (9.6 vs. 8.2%;  $p = 0.739$ , AF vs. no-AF, respectively). In the multivariable analysis, factors associated with higher mortality were: age, male, valvular aetiology, uric acid, and comorbidity. In the analysis of the subgroup with HFpEF with AF, the presence of chronic AF compared to de novo AF was associated with higher mortality (HR 1716; 95% CI 1099–2681;  $p = 0.018$ ).

**Conclusions:** In patients with HFpEF, the presence of AF is frequent. During the one-year follow-up, the presence of AF does not influence mortality or readmissions in patients with HFpEF.

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◇ The names of the RICA research group members are included in Appendix A.

## Influencia de la fibrilación auricular en la mortalidad de los pacientes con insuficiencia cardiaca con fracción de eyección preservada

### RESUMEN

#### Palabras clave:

Insuficiencia cardiaca  
Fracción de eyección preservada  
Fibrilación auricular  
Mortalidad  
Reingreso

**Introducción y objetivos:** La información del impacto de la fibrilación auricular (FA) en el pronóstico de los pacientes con insuficiencia cardiaca con fracción de eyección preservada (IC-FEP) es controvertido. Se analizó el pronóstico en cuanto a la mortalidad y los reingresos al año de los pacientes con IC-FEP y FA. **Métodos:** Estudio observacional y prospectivo en 1.971 pacientes con IC-FEP, que presentan un ingreso por IC aguda. Los pacientes se dividieron en 2 grupos según la presencia o no de FA. Analizamos la mortalidad, los reingresos y el combinado mortalidad/reingresos al año de seguimiento.

**Resultados:** Un total de 1.177 (59%) pacientes presentaban FA, con una edad media de 80,3 (7,8) años, y de ellos, 1.233 (63%) eran mujeres. El paciente con IC-FEP y FA tenía una mayor edad, era del sexo femenino y presentaba más frecuentemente un origen valvular y una menor comorbilidad medida por el índice de Charlson. Al año de seguimiento, 430 (22%) pacientes murieron y 840 (43%) fueron reingresados. Entre los 2 grupos analizados no hubo diferencia en la mortalidad por todas las causas (22 vs. 21%;  $p = 0,739$ , FA vs. no FA, respectivamente) ni por causas cardiovasculares (9,6 vs. 8,2%;  $p = 0,739$ , FA vs. no FA, respectivamente). En el análisis multivariable se asociaron con mayor mortalidad: la edad, el sexo masculino, la etiología valvular, la hiperuricemia y la comorbilidad. En el análisis del subgrupo con IC-FEP con FA, la presencia de FA crónica comparada con la FA de novo se asoció con una mayor mortalidad (HR 1,716; IC 95% 1,099-2,681;  $p = 0,018$ ).

**Conclusiones:** En pacientes con IC-FEP es frecuente la presencia de FA. Durante el seguimiento a un año, la presencia de FA no influye en la mortalidad ni en los reingresos hospitalarios en pacientes con IC-FEP.

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### Introduction

Heart failure (HF) is a growing global epidemic, with a prevalence of 1–2% of the adult population in developed countries, increasing to more than 10% in people over 75 years of age.<sup>1</sup> Currently, it is estimated that more than 50% of patients with HF have preserved left ventricular ejection fraction (HFpEF), understood as  $\geq 50\%$ , thereby becoming a very prevalent form of HF, with high mortality and hospital readmissions.<sup>2,3</sup>

Atrial fibrillation (AF) is the most common arrhythmia in HF, with both preserved and reduced ejection fraction, worsening the symptoms and increasing the risk of cardioembolic episodes.<sup>4</sup> The appearance of AF in HF has prognostic implications, probably because it is an indicator of greater structural deterioration in the heart.<sup>5</sup> On the other hand, AF can lead to the development of HF due to tachycardiomyopathy, obtaining a better prognosis when the ventricular rate is controlled.<sup>6</sup> A higher prevalence of AF has been described in patients with HFpEF, compared with those with reduced ejection fraction (HFrEF).<sup>7,8</sup> Several studies have tried to clarify the prognostic role of AF in HF, with very different results; some give evidence of a worse prognosis in HFrEF,<sup>9</sup> however, in others, AF was not an independent predictor of mortality.<sup>10,11</sup>

The objective of the study is to evaluate the impact on mortality and hospital readmissions of AF at one-year follow-up, in a group of patients with HFpEF, participants in a multicenter prospective study representative of standard clinical practice.

### Methods

#### Study sample

The patients included in the study were registered in the RICA national registry of HF coordinated by the Working Group of Heart Failure of the Spanish Society of Internal Medicine. Medicine. This is a multicenter, prospective registry, which includes 1971 patients consecutively admitted for acute HF (AHF) in Internal Medicine departments of 52 Spanish hospitals.<sup>12,13</sup> The Clinical Research Ethics Committee of the Reina Sofia University Hospital of Córdoba approved the protocols for data collection, and all patients gave their informed consent to be included.

#### Study population

We included patients aged 50 years or older admitted because of AHF, according to the diagnostic criteria of the European Society of Cardiology.<sup>14</sup> Patients who died during hospital admission were excluded. For this study, all patients who had HFpEF ( $\geq 50\%$ ) were evaluated. Follow-up after hospital discharge consisted of 2 follow-up visits at 3 and 12 months.

#### Objectives

The primary endpoints of our study were to evaluate all causes of death, readmissions and combined mortality/readmissions during one-year follow-up. The patients (or their relatives) were contacted when they did not attend the follow-up visits, in order to determine the causes and the patients' clinical situations. Subsequent admissions were coded as readmissions. Secondary endpoints included the description of the clinical characteristics, the phenotype and the patient's viewpoint of the "standard clinical practice" regarding the treatment of AF and the HFpEF of our cohort.

#### Variables

The data was recorded in detail through a website (<https://www.registorica.org>) which contained the main database to which researchers had access using a personal password. Confidentiality was respected, since no personal data were stored, except for the date of birth and the initials of the name to avoid duplication of data.

The registry included: sociodemographic data, pathological background, comorbidities (Charlson index), baseline functional status for basic activities of daily living (Barthel index), clinical data upon admission (blood pressure, heart rate, weight and height, body mass, characteristics of decompensation, provoking factors) and the prescription of medications. With respect to the clinical severity of HF, the functional class was measured using the *New York Heart Association* (NYHA) scale, and the left ventricular ejection fraction was evaluated using echocardiography 2D and electrocardiogram alterations. Analytical determinations included complete blood count, renal function, lipids, glucose, uric acid,

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