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Comorbidities, Fragility, and Quality of Life in Heart Failure Patients With Midrange Ejection Fraction

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Abstract

Objective: To assess the effects of comorbidities, fragility, and quality of life (QOL) on long-term prognosis in ambulatory patients with heart failure (HF) with midrange left ventricular ejection fraction (HFmrEF), an unexplored area.

Patients and Methods: Consecutive patients prospectively evaluated at an HF clinic between August 1, 2001, and December 31, 2015, were retrospectively analyzed on the basis of left ventricular ejection fraction category. We compared patients with HFmrEF (n=185) to those with reduced (HFrEF; n=1058) and preserved (HFpEF; n=162) ejection fraction. Fragility was defined as 1 or more abnormal evaluations on 4 standardized geriatric scales (Barthel Index, Older Americans Resources and Services scale, Pfeiffer Test, and abbreviated-Geriatric Depression Scale). The QOL was assessed with the Minnesota Living with Heart Failure Questionnaire. A comorbidity score (0-7) was constructed. All-cause death, HF-related hospitalization, and the composite end point of both were assessed.

Results: Comorbidities and QOL scores were similar in HFmrEF (2.41±1.5 and 30.1±18.3, respectively) and HFrEF (2.30±1.4 and 30.8±18.5, respectively) and were higher in HFpEF (3.02±1.5, $P<.001$, and 36.5±20.7, $P=.003$, respectively). No statistically significant differences in fragility between HFmrEF (48.6%) and HFrEF (41.9%) ($P=.09$) nor HFpEF (54.3%) ($P=.29$) were found. In univariate analysis, the association of comorbidities, QOL, and fragility with the 3 end points was higher for HFmrEF than for HFrEF and HFpEF. In multivariate analysis, comorbidities were independently associated with the 3 end points ($P\leq.001$), and fragility was independently associated with all-cause death and the composite end point ($P<.001$) in HFmrEF.

Conclusion: Comorbidities and fragility are independent predictors of outcomes in ambulatory patients with HFmrHF and should be considered in the routine clinical assessment of HFmrEF.

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Heart failure (HF) is a chronic condition associated with frequent hospital admissions and poor prognosis. In developed countries, 1% to 2% of the adult population has HF, and this prevalence rises to 10% or more in those aged 70 years and older.[1] The signs and symptoms of HF substantially impair patients' quality of life (QOL). Patients with HF frequently have comorbidities that contribute to increased morbidity and mortality and further impair their QOL.[2] The most prevalent comorbidities are chronic kidney disease, anemia, and diabetes, which are independently associated with a higher risk of mortality and/or HF hospitalization.[2]

Patients with HF often have coexisting fragility. Indeed, even young patients with HF show a high degree of fragility,[3-5] which

also contributes to QOL impairment.[5] In this context, QOL is related to fragility in the full age spectrum of patients with HF.[5] Notably, there is still no universal definition of fragility; thus, there are no fully standardized methods for measuring it, although several tools are increasingly used in recent times.[6] We started to assess fragility almost 2 decades ago in ambulatory patients with HF using a set of validated geriatric scales as surrogates of fragility,[3,5] and with these scales we have shown that fragility is a key determinant for the prognosis of patients with HF of all ages.[7]

The 2016 HF European Society of Cardiology Guidelines suggest that more investigation is needed to characterize the newly defined subgroup of patients with heart failure and mildly reduced left ventricular ejection fraction (HFmrEF).[8] These patients, in whom the left ventricular ejection fraction (LVEF) ranges from 40% to 49%, comprise a gray area between patients with HF with reduced ejection fraction (HFrEF) and patients with HF with preserved ejection fraction (HFpEF). Accordingly, the present study aimed to assess the association of fragility, comorbidities, and QOL on the long-term prognosis of ambulatory patients with HFmrEF and to compare the characteristics of patients with HFmrEF with those of patients with HFrEF and patients with HFpEF.

PATIENTS AND METHODS

Study Population

The study included consecutive ambulatory patients who were referred to a structured HF clinic at a university hospital between August 1, 2001, and December 31, 2015. The clinical practice criteria for referral to the HF clinic have been reported elsewhere[5,9-11] and were irrespective of etiology (at least 1 HF hospitalization and/or reduced LVEF <40%). The patients, their clinical characteristics, and the events during follow-up were prospectively acquired, but the current analysis was retrospectively performed on the basis of new classification of the European Society of Cardiology.

All patients provide written informed consent at their first (baseline) visit for the collection of samples for analysis and for the use of their clinical data for research purposes. The study was approved by the local ethics committee and undertaken in compliance with the principles of the Declaration of Helsinki.

Categorization of LVEF

Patients were categorized according to the baseline LVEF at first visit in HFrEF (LVEF, <40%), HFmrEF (LVEF, 40%-49%), and HFpEF (LVEF, ≥50%), independently of how was the LVEF evolution during follow-up.

Assessment of QOL

The QOL was assessed at the baseline visit using the Spanish version of an HF-specific questionnaire, the Minnesota Living with Heart Failure Questionnaire (MLHFQ),[12] which is widely used[13] and has been prospectively validated in Spain.[14,15] The MLHFQ consists of 21 questions and evaluates the impact of HF on the physical, psychological, and social aspects of patients' lives. The responses range from 0 (no limitation) to 5 (maximal limitation); thus, the global scores can range from 0 to 105, with higher scores reflecting worse QOL. Depending on the patient's reading and writing capabilities, an HF clinic nurse helped the patient complete the questionnaire[13] without altering the patient's response or compromising the patient's independence.

Fragility Assessment

Fragility was assessed at baseline using a basic geriatric evaluation with 4 standardized geriatric scales.[3,5,7] The Barthel Index[16] evaluates independence in performing basic activities of daily living (range, 0-100); the Older Americans Resources and Services (OARS) Scale (the Instrumental Activities Daily Living subscale of the Multidimensional Functional Assessment Questionnaire)[17] evaluates autonomy in performing instrumental activities of daily living (range, 0-14); the Pfeiffer Test (Short Portable Mental Status Questionnaire)[18] evaluates cognitive function (range, 0-10); and the abbreviated Geriatric Depression Scale (GDS)[19] identifies possible emotional problems. Fragility was defined as having at least 1 abnormal evaluation on any of these 4 scales.

The predefined criteria for abnormal results for the scales were as follows[3,5,7]: Barthel Index,