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The frailty syndrome is associated with adverse health outcomes in very old patients with stable heart failure: A prospective study in six Spanish hospitals☆

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ABSTRACT

Background: Most studies on the association between the frailty syndrome and adverse health outcomes in patients with heart failure (HF) have used non-standard definitions of frailty. This study examined the association of frailty, diagnosed by well-accepted criteria, with mortality, readmission and functional decline in very old ambulatory patients with HF.

Methods: Prospective study with 497 patients in six Spanish hospitals and followed up during one year. Mean (SD) age was 85.2 (7.3) years, and 79.3% had LVEF > 45%. Frailty was diagnosed as having ≥ 3 of the 5 Fried criteria. Readmission was defined as a new episode of hospitalisation lasting > 24 h, and functional decline as an incident limitation in any activity of daily living at the 1-year visit. Statistical analyses were performed with Cox and logistic regression, as appropriate, and adjusted for the main prognostic factors at baseline.

Results: At baseline, 57.5% of patients were frail. The adjusted hazard ratio (95% confidence interval) for mortality among frail versus non-frail patients was 1.93 (1.20–3.27). Mortality was higher among patients with low physical activity [1.64 (1.10–2.45)] or exhaustion [1.83 (1.21–2.77)]. Frailty was linked to increased risk of readmission [1.66 (1.17–2.36)] and functional decline [odds ratio 1.67 (1.01–2.79)]. Slow gait speed was related to functional decline [odds ratio 3.59 (1.75–7.34)]. A higher number of frailty criteria was associated with a higher risk of the three study outcomes (P trend < 0.01 in each outcome).

Conclusions: Frailty was associated with increased risk of 1-year mortality, hospital readmission and functional decline among older ambulatory patients with HF.

Abbreviations: ADL, Activities of Daily Living; CGA, Comprehensive Geriatric Assessment; CHS, Cardiovascular Health Study; IADL, Instrumental Activities of Daily Living; NYHA, New York Heart Association; MDRD, Modified Diet in Renal Disease formula; MEC, Mini-Mental State Examination; NTproBNP, N-terminal pro-brain natriuretic peptide; PASE, Physical Activity Scale for the Elderly.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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1. Introduction

Frailty is an age-associated medical syndrome characterised by increased vulnerability to even minor stressors, which manifests as higher risk of adverse health outcomes including disability, hospitalisation and death [1,2]. And heart failure (HF) is the most common cause of hospital admission in individuals aged 65 years or older and shows a high risk of mortality, disability and hospital readmission [3–6].

Of note is that frailty and HF are frequently associated [7]; indeed, it has been suggested that these two syndromes share common pathogenic mechanisms [8] and that some treatment modalities, such us physical exercise, benefit both of them [9–10]. Very old patients with HF show a high prevalence of frailty and disability [11–13], and their mortality depends on the degree of functional and cognitive impairment [14–16] ; moreover frailty has also been linked to greater functional decline and higher risk of hospital readmission and death in these patients [9,11,17–19].

However, knowledge of the prognostic relevance of frailty in HF is rather limited. In fact, some studies have included relatively young patients with a mean age of 66–68 years, who mostly had reduced left-ventricle ejection fraction (LVEF) [12,20–21]. In other investigations, patients were recruited during a hospitalisation episode [11,14,19, 22–23], which may contribute to deconditioning and increase the frequency of frailty. Moreover, several studies only selected patients in good functional condition [11], or in specific settings like the community [24] and cardiology clinics [20–21]. And most importantly, a number of investigations used non-standard definitions of frailty, such as disability, functional decline or cognitive impairment [14,20–21,24], and other studies simply focused on indicators or individual components of the frailty phenotype [6,25–27].

Thus, the influence of frailty, based on widely-accepted diagnostic criteria, on the prognosis of very old patients with stable HF is still uncertain. Accordingly, we examined the association of the frailty syndrome with mortality, readmission and functional decline in very old ambulatory patients after a hospital discharge for HF.

2. Methods

2.1. Study design and participants

This study was conducted with ambulatory patients discharged from six Spanish hospitals with a main diagnosis of HF from December 1, 2010 to November 30, 2012. Patients were previously admitted to the Geriatric Medicine or Cardiology departments, and referred to the Geriatric Medicine specialised outpatient clinic when they met the following inclusion criteria: a) age ≥ 75 years on recruitment; b) HF diagnosis according to Framingham [28] and European Society of Cardiology [29] criteria; c) having had a hospitalisation with the main discharge diagnosis of HF in the last twelve months; and d) substantial comorbidity, based on a Charlson index ≥3 [30]. HF criteria in each patient were assessed by cardiologists and geriatricians.

Exclusion criteria were: a) terminal illness with a life expectancy <-5 months according to the researcher's opinion; b) functional or cognitive impairment that limited the patient in attending follow-up visits or completing the study questionnaires; c) being on a waiting list for any invasive cardiac procedure; and d) difficulty of follow-up due to other reasons such as moving out of the hospital area.

Informed written consent was given by study participants, and the study protocol was approved by the local institutional review board.

2.2. Study variables

We collected standard sociodemographic and biomedical variables as well as data from a comprehensive geriatric assessment (CGA).

Sociodemographic variables included age, gender, cohabitation, and educational level. Biomedical variables comprised cardiovascular risk factors, comorbidities and the Charlson index, HF aetiology, NYHA functional class, LVEF measured with transthoracic echocardiography, laboratory measures including glomerular filtration rate as estimated with the Modified Diet in Renal Disease formula (MDRD) [31], weight and height, blood pressure, heart rate, and active drug treatment on recruitment.

The CGA included: a) Cognitive function as per the Spanish adaptation of the Mini-Mental State Examination (MEC) [32]; b) Depression, with the 15-item Yesavage Geriatric Depression Scale [33]; c) Limitations in activities of daily living (ADL) based on the Katz index [34], and in instrumental activities of daily living (IADL) with the Lawton and Brody index [35]; d) Mobility limitation based on this scale: 1, no walking limitation; 2, use of a walking cane or stick; 3, use of a Zimmer frame or needing help from one person; and 4, wheelchair-bound or needing help from two people for ambulation; e) Health-related quality of life, assessed with the Minnesota Living with Heart Failure Questionnaire [36]; and f) Frailty, assessed with the 5 phenotypic criteria proposed by Fried et al. in the Cardiovascular Health Study (CHS) [2]: 1) muscle weakness, based on the CHS cut-points of grip strength, measured with a Jamar type dynamometer on the dominant hand; three measurements were performed and the highest value was selected; 2) slowness, according to the CHS cut-points of slow gait speed measured on a 15-feet distance without acceleration period, and patients unable to walk were considered to meet the slowness criterion; 3) low physical activity, as assessed with the Physical Activity Scale for the Elderly (PASE) questionnaire [37], the cut point was the lowest quintile, which corresponded to a score of 0, that is, less than half an hour walking outside the home on a daily basis; 4) exhaustion, based on a positive answer to any of two questions taken from the Centre for Epidemiologic Studies Depression Scale: "Have you felt that everything you did was a big effort?" and "Have you felt that you could not keep on doing things?" at least 3–4 days a week [38]; and 5) unintentional weight loss ≥4.5 kg or ≥5% of body weight in the last year. Individuals were classified as frail when they had ≥3 criteria, as pre-frail when having 1–2, and as robust when no criterion was present. For this analysis, robust and pre-frail patients were grouped as non-frail. The "timed get-up and go" test [39] was recorded in all patients with the ability to walk.

In order to attenuate the influence of hospitalisation-related deconditioning on functional and frailty measures, the recruitment visit was done at least one month after hospital discharge.

2.3. Study outcomes

Study participants were prospectively followed up during one year. Follow-up started on the day when the CGA was performed and ended on the 1-year visit, the date of death, or the date of last contact (in those lost to follow-up), whichever came first. Study outcomes were all-cause death, readmission, and incident functional limitation during follow-up. Readmission was defined as an episode of hospitalisation lasting >24 h, and the analysis was done considering the time to the first readmission. Incident functional limitation was any newly developed limitation in ADL assessed at the 1-year visit. Data on study outcomes were collected at the 1-year follow-up visit (where the CGA was performed again), through review of the electronic clinical chart, and from telephone interview with patient and relatives.

2.4. Statistical analysis

From the 507 study participants we excluded 10 who lacked complete information on frailty (Supplementary Fig. 1). Thus, analyses were conducted with 497 patients, of whom 286 (57.5%) were frail at baseline. Descriptive analyses were performed using percentages for categorical variables and the mean ± standard deviation (SD) for continuous variables. Differences in sociodemographic, biomedical and CGA variables between frail and non-frail patients were assessed with a chi-square test for categorical variables, and the Student's *t*-test for continuous variables.