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Brief Report

Frailty Assessment in Advanced Heart Failure

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ABSTRACT

Background: Several studies have recently demonstrated the value of frailty assessment in a general heart failure (HF) population; however, it is unknown whether these findings are also applicable in advanced HF. We investigated the utility of frailty assessment and its prognostic value in elderly patients with advanced HF.

Methods: Forty consecutive elderly subjects aged ≥65 years, with left ventricular ejection fraction ≤35%, New York Heart Association class III or IV, and a 6-minute walk test <300 m were enrolled from the HF clinic at Montefiore Medical Center between October 2012 and July 2013. Subjects were assessed for frailty with the Fried Frailty Index, consisting of 5 components: hand grip strength, 15-foot walk time, weight loss, physical activity, and exhaustion. All subjects were prospectively followed for death or hospitalization.

Results: At baseline, the mean age of the cohort was 74.9 ± 6.5 years, 58% female, left ventricular ejection fraction 25.6 ± 6.4%, 6-minute walk test 195.8 ± 74.3 m and length of follow-up 454 ± 186 days. Thirty-five percent were prefrail and 65% were frail. Frailty status was associated with the combined primary endpoint of mortality and all-cause hospitalization (hazard ratio [HR] 1.93, 95% confidence interval [CI] 1.15–3.25, $P = .013$). On individual analysis, frailty was associated with all-cause hospitalizations (HR 1.92, 95% CI 1.12–3.27, $P = .017$) and non-HF hospitalizations (HR 3.31, 95% CI 1.14- 9.6, $P = .028$), but was not associated with HF hospitalizations alone (HR 1.31, 95% CI 0.68–2.49, $P = .380$).

Conclusions: Frailty assessment in patients with advanced HF is feasible and provides prognostic value. These findings warrant validation in a larger cohort. (*J Cardiac Fail 2016;*■■:■■–■■)

Key Words: Frailty, heart failure, elderly, advanced heart failure, hospitalization, mortality.

Frailty is a biological syndrome defined as a decreased homeostatic reserve leading to an increased vulnerability to stressors and adverse outcomes.[1] Frailty manifests clinically as a disproportionate change in health status in response to a physical or psychological stress.[2] Several recent studies in the general heart failure (HF) population have demonstrated that frailty is associated with increased health care utilization, hospitalizations, mortality,[3–5] and incident HF.[6] When HF reaches more advanced states, it manifests similar to frailty, as a biological syndrome where the primary insult is cardiac dysfunction but leads to systemic consequences. Because of this significant overlap, the utility of frailty assessment in advanced HF is unclear. The aim of the current study was to investigate the utility of frailty assessment and its prognostic value in elderly patients with advanced HF.

Methods

In this single-center pilot study, consecutive patients from Montefiore Medical Center HF Clinic, between October 2012 and July 2013, aged ≥65 years, New York Heart Association (NYHA) class III or IV, and left ventricular ejection fraction (LVEF) ≤ 35% (measured by echocardiogram within 30 days of the study visit) were screened to participate. Key

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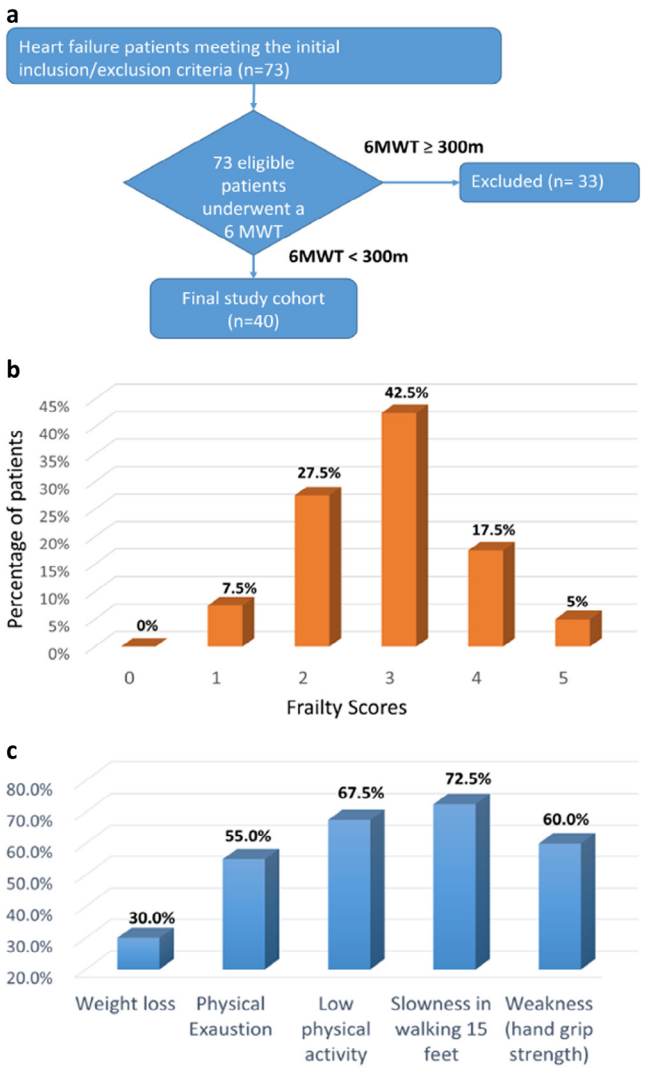

Fig. 1. (A) Flowchart describing the patient selection process towards achieving the final study cohort of 40 patients. (B) Spectrum of frailty: percentage of patients with different frailty scores (range 0–5). (C) Percentage of patients meeting frailty criteria for each of the individual components of the Fried Frailty Index. LVEF, left ventricular ejection fraction; 6MWT = 6 minute walk test.

exclusion criteria included duration of HF < 6 months, acute decompensation within the previous 30 days, or inability to walk. Patients who met these inclusion/exclusion criteria underwent a 6-minute walk test (6MWT) and were enrolled in the final study cohort only if they walked <300 m (Fig. 1a). Hence, for the purposes of this study, advanced HF was defined as "NYHA class III or IV, LVEF ≤35%, and a 6MWT of <300 m." The cutoff of <300m on 6MWT was chosen because it has been shown to define an increased risk of adverse events in HF.[7] The study was approved by the Albert Einstein College of Medicine Institutional Review Board.

Frailty was assessed using a modified version of the Fried Frailty Index as defined in the Cardiovascular Health Study.[2] Five domains were assessed for frailty: weight loss, exhaustion, weakness, slow gait, and reduced physical activity. Each domain was scored 0 or 1 based on its absence or presence and combined for a composite score of 0 to 5. Subjects with a score of 0 were classified as "not frail," 1–2 as "prefrail," and 3 or higher as "frail." Assessment of the individual domains is described in the supplementary Table S1.

All subjects were followed from the time of testing through August 2014 for the combined primary endpoint of all-cause hospitalizations or death. Secondary endpoints included all-cause mortality, non-HF hospitalizations, and HF-related hospitalizations only. Outcomes were ascertained through review of medical records and confirmed by telephone follow-up.

Statistical Analysis

Baseline characteristics were described as frequencies for categorical and as mean ± standard deviation for continuous variables, and compared using chi-squared test and unpaired *t* test, respectively. Cox proportional hazards ratio (HR) modified for Andersen-Gill modeling was calculated to test the effect of frailty on hospitalizations and mortality, and adjusted for covariates. Unlike the traditional Cox model, which accounts for only the first hospitalization, the Andersen-Gill model takes into account multiple hospitalizations[8,9] and treats each hospitalization for each subject as a separate observation. Statistical analysis was performed using R statistical software and 2-tailed *P* values of <.05 were considered significant.

Results

Seventy-three subjects met the initial criteria and underwent 6MWT. Of these, 40 walked <300 m and formed the final study cohort (Fig. 1a). Overall characteristics included, mean age of 74.9 ± 6.5 years, 58% female, 37.5% NYHA class IV, LVEF 25.6 ± 6.4%, 6MWT 195.8 ± 74.3 m, and Charlson Comorbidity Index (CCI) score of 4.9 ± 1.9. There was a spectrum of frailty scores, ranging from 0 to 5 (Fig. 1b). The proportion of subjects meeting frailty criteria for each of the individual components is shown in Fig. 1c.

When graded according to the prespecified Fried criteria: 0 subjects were not frail, 14 (35%) were prefrail, and 26 (65%) were frail. The baseline demographics of the overall cohort and as analyzed by the prefrail and frail groups are shown in Table 1. There was a higher prevalence of diabetes in the prefrail group; otherwise, there were no significant differences in the baseline characteristics. Both groups were equally well medicated and the length of follow up was similar.

Frailty and Outcomes

During follow-up, 10 patients died and 26 were hospitalized for any cause, including 20 for an exacerbation of HF. Including repeated events, there were a total of 69 all-cause hospitalizations, 45 (65%) of which were due to HF exacerbations. Pneumonia, infections and gastrointestinal bleeding were the major causes of non-HF hospitalizations. Of the 10