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# The simpler modified fried frailty scale predicts 2-year mortality in older adults with heart failure: a pilot study

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## Abstract

**Objective** The Simpler Modified Fried Frailty Scale (*SMFFS*) has recently been developed from the original Fried scale to ease its use in clinical practice, by transforming the items requiring measurements into the self-reported inquiries. Its predictive validity needs to be clarified, especially in populations with a high prevalence of frailty, such as patients with heart failure (HF). Primary aim of this study is to find out the prevalence of frailty in older patients with HF by using *SMFFS* and show its concordance with other frailty assessment tools. Secondary aim is to reveal whether *SMFFS* is useful to predict mortality in follow-up.

**Method** This is a prospective, follow-up study including older adults (≥ 65 years) with HF. *SMFFS* was used to assess frailty phenotype and presence of ≥ 3 items was accepted as frailty. *FRAIL* scale, the Study of Osteoporosis Fractures (*SOF*) index, and Edmonton Frailty Scale (*EFS*) were alternatively used to study the correlation of *SMFFS* with different scales. Cox-regression analysis was performed to identify whether *SMFFS*-defined frailty could predict mortality in follow-up, with adjusting for a list of clinical characteristics and geriatric syndromes.

**Findings** Among 101 patients with HF, 44 (42.8%) were female. Mean age was 75.8 ± 7.6 and frailty prevalence was 63.4% according to *SMFFS*. *SMFFS* showed a strong correlation with the other frailty scales. In a median follow-up of 759 days, cardiomegaly, increased pulmonary artery pressure (PAP) and frailty defined by *SMFFS* were the only predictors of mortality in older adults with HF after adjustments for age, falls in the previous year, undernutrition, probable sarcopenia, functional impairments, and quality of life [HR (95% CI) were 3.88 (1.05–14.3), 1.05 (1.01–1.09), and 10.96 (1.07–112.05) ($p = 0.027$); for older age, PAP, and frailty, respectively].

**Conclusions** As a self-reported screening tool, *SMFFS* was independently associated with mortality in a median follow-up of two years. Frailty assessment recommended by the guidelines for risk stratification in patients with HF seems to be more effectively integrated into routine HF practice with the use of the easy and practical *SMFFS*. Further large scale studies are needed to support the predictive validity of *SMFFS* in older patients with HF.

**Keywords** Frailty, Heart failure, Mortality, Older adults, Sarcopenia

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## Introduction

Heart failure (HF) is an important global health problem associated with increase in hospitalizations, medical expenses, morbidity, and mortality. Despite numerous disease-specific strategies, HF management is still challenging and HF-related adverse outcomes are persistently high [1]. Besides disease's nature, it is noticeable that non-cardiac factors also have an impact on this reality. In fact, it has been reported that the most common cause of recurrent hospitalizations in HF patients is non-cardiac reasons [2]. In this context, the concept of frailty, which has been mentioned more and more frequently in recent years among the factors determining HF prognosis, is considered as a risk-modifying and "needs-to-control" parameter in current guidelines [3, 4].

Frailty in patients with HF was defined as "a multidimensional dynamic state, independent of age, that makes the individual with HF more vulnerable to the effect of stressors" [5]. It is noteworthy that although frailty is known as a geriatric syndrome, it can also be seen regardless of chronological age, and is actually considered as "biological aging" due to the decrease in the reserves that constitute the physiology. Frailty and HF have a bidirectional relationship: Independent of age and functional class, almost half of the patients with HF were reported to be frail [6] and frail individuals had an increased risk of developing HF [7]. The overlapping phenotypic characteristics of both concepts are related to the shared pathophysiological pathways like dysregulation in neurohormonal activation, metabolic, and inflammatory pathways [8]. Most importantly, frail patients with HF have a worse prognosis compared to non-frail patients. Therefore it is considered as a strong and independent predictor of adverse outcomes and reported to improve traditional risk scores when included in the evaluation of patients with HF [9, 10].

Current HF guidelines state that frailty should be assessed to determine treatment decisions, calibrate treatment goals, define the support needed for the self-care and treatment adherence, and organize the follow-up process [3, 4]. Although there are various frailty assessment tools are available, the optimum scale in patients with HF has not yet been elucidated. The 2022 AHA/ACC/HFSA Guide for HF and recently published "Frailty in Advanced HF Position Paper" endorsed by International Society for Heart and Lung Transplantation recommended the use of Fried Frailty Scale (FFS) for the assessment of frailty in the basis of HF [3, 8]. However, FFS requires measurements of muscle strength, gait speed, and physical activity, which hampers frailty assessment from being integrated into routine clinical practice in many already busy cardiology and geriatrics clinics. Based on this limitation of the FFS, items that require objective measurements have been converted into subjective questions answered by the patient or their caregivers/relatives [namely "the Simpler Modified FFS (*SMFFS*)] and have previously been shown to predict mortality in nursing home residents [11]. Here, we aimed to study *i. the prevalence of frailty in older patients with HF by SMFFS, ii. the correlation of SMFFS with other common frailty assessment tools*, and *iii. whether baseline frailty defined by SMFFS is capable of predicting all-cause mortality in follow-up in patients with HF.*

## Materials and methods

We conducted this pilot, prospective cohort study on patients aged ≥ 65 years with HF who admitted to our tertiary health center on a scheduled basis or with exacerbation between February 2021 and March 2022. Exclusion criteria were: (i) Presence of conditions that may significantly affect the prognosis during follow-up (acute coronary syndrome, stroke in the last 3 months, active neoplasms, etc.), (ii) Neuropsychiatric conditions (i.e., severe cognitive impairment or depression, delirium, etc.) or sensory (visual/hearing) impairments that may prevent the application of questionnaires and impair the reliability of measurements, (iii) Conditions that may prevent reliable handgrip strength (HGS) measurement (i.e., stroke, hand osteoarthritis, peripheric artery disease, or neuropathy), (iv) Lack of consent to participate in the study.

### Sample size estimation

The overall estimated frailty prevalence was reported to be 44.5% in older patients with HF, according to a meta-analysis including a total of 26 studies [6]. Based on this prevalence and with an error probability of 10%, we calculated a minimum sample size of 95 [12].

### Data collection

We collected data on demographic and clinical variables through face-to-face interviews and medical records in patient files: age, sex, smoking status, duration of CHF diagnosis, Charlson Comorbidity Index (CCI), regular medications, number of hospitalizations during the previous year, the N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) value (pg/ml) measured closest to the assessment date, and echocardiographic parameters [pulmonary artery pressure (PAP) (mmHg), presence of abnormal wall motion (akinesia or hypokinesia), cardiomegaly, ventricular dilatation, and left ventricular ejection fraction (LVEF) (%)]. Transthoracic echocardiographies (TTE) of patients receiving inpatient treatment were evaluated during their hospitalization. For outpatients, the latest TTEs evaluated within the last 6 months were accessed from medical records. Based on the measurement of LVEF, participants were classified as: *HF with reduced EF (HFrEF)* (LVEF ≤ 40%), *HF*

*with mildy-reduced EF (HFmrEF)* (LVEF between 41 and 49%), and *HF with preserved EF (HFpEF)* (LVEF ≥ 50%), as suggested by the 2021 European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic HF [4].

#### Frailty assessment

Since our hypothesis was that frailty detected by the *SMFFS* was valid in predicting mortality in follow-up, the primary frailty screening tool we used was the *SMFFS*. To evaluate the correlation of the *SMFFS* with other screening tools, we used three more frailty scales recommended by guidelines for use in the frailty assessment in the older adults: FRAIL scale, the Study of Osteoporosis Fractures (SOF) index, and Edmonton Frailty Scale (EFS) [13–15].

Frailty was first described by Fried and colleagues and objectively identified by FFS as the presence of three or more of five characteristics of a "frail" phenotype: Unintentional weight loss (10 lbs in prior year), self-reported exhaustion, weakness, slowness, and low physical activity. This definition was independently predictive of falls, disabilities, hospitalizations, and mortality [16]. However, measurement of handgrip strength adjusted for sex and body mass index (BMI) and time to walk 15 feet adjusted for sex and standing height, and calculation of kilocalories expended per week are the rate-limiting steps which restrict its widespread use. Our study group transformed the items requiring measurements into self-reported assessments questioning whether the respondents judge that their grip strength, walking speed, and physical activity decreased compared to the same-aged healthy individuals (Supplementary table) [17]. Scoring system was the same as the original FFS: 0: robust, 1–2 points: pre-frail, ≥ 3 points: frail. This definition succeeded to predict mortality in nursing home residents in a median of 46-month follow-up previously [11].

The 5-item *FRAIL* (**F**atigue, **R**esistance, **A**mbulation, **I**llness, and **L**oss of weight) scale is a screening tool for physical frailty, representing biological (fatigue and weight loss) and functional factors (weakness and slow gait speed), and deficit accumulation by illness. The scoring system of the *FRAIL* scale is the same as the *FFS* (0: robust, 1–2 points: pre-frail, ≥ 3 points: frail) [18]. The *SOF* index is another physical frailty assessment tool representing biological (weight loss) and functional factors (reduced energy level and inability to complete five chair rises), with a scoring system of 0: robustness, 1: pre-frailty, and 2–3: frailty [19]. The *EFS* represents multidimensional frailty assessment by addressing physical, psycho-cognitive, and social domains of frailty concept. It is a validated tool with 2 practical tasks and 9 closed questions and evaluates general health status, functional independence, nutrition, continence, regular medication use, physical performance, cognition, mood, and social support. In order to assess cognitive status, we used clock drawing test. Physical performance was assessed by the Timed Up-and-Go (TUG) Test and participants were asked to rise from a standart chair with an approximate seat height 46 cm, walk to a marker 3 m away, turn around, walk back and sit down again. The *EFS* was scored as 0–4 points: robust, 5–6: vulnerable, and ≥ 7 points: frail [20]. Patients identified as frail were referred to the geriatrics team to identify potentially reversible causes and to apply appropriate interventions.

#### Comprehensive geriatric assessment

We assessed falls in the previous year, malnutrition, sarcopenia, functionality status, polypharmacy, and quality of life (QoL). We evaluated nutritional status with the Mini-Nutritional Assessment-Short Form (MNA-SF). MNA-SF is a six-item practical and validated tool for screening of malnutrition and assesses "decline in food intake, weight loss, mobility, psychological stress, neuropsychological problems, and BMI". We defined a score of ≥ 12 points as normal nutritional status, and scores below 12 as undernutrition [21]. We used SARC-F questionnaire to assess the risk of sarcopenia. It consists of five items assessing "**S**trength, **A**mbulation, **R**esistance, **C**limbing stairs, and **F**alls in the past year". A total score of ≥ 4 indicates an increased risk of sarcopenia [22]. We used "probable sarcopenia" definition suggested by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) consensus paper for sarcopenia diagnosis [23]. We measured HGS of the participants via Jamar hydraulic hand dynamometer while the participants were sitting, elbows in 90∘ flexion, and wrist in a neutral position. The participants instructed to apply maximum grip strength with both hands, separately and sequentially. We considered the maximal grip strength as the measured HGS value [24]. We used the thresholds recommended by the EWGSOP2 for the diagnosis of probable sarcopenia (i.e., HGS < 27/16 kg for males and females, respectively) [23].

We assessed basic and instrumental activities of daily living (ADL and IADL) with Katz and Lawton scales [25, 26]. The Katz scale questions six domains of functionality, i.e., bathing, dressing, eating, incontinence, toileting, and transfer. The Lawton Scale questions eight domains of IADLs, i.e., meal preparation, housekeeping, laundering, shopping, telephone use, transportation, medications use, and budgeting. For both scales, each activity performed without assistance were scored 1 point and activity could not be performed or could only performed with assistance was scored 0 point. Limitation in ADL or IADL was defined as having at least one disability in any of the ADL or IADL domains [27].

We checked regularly used medications and supplements and defined polypharmacy as taking ≥ 5

medications per day. We evaluated QoL using EuroQol-5 Dimension-3 Levels questionnaire (EQ-5D-3 L) descriptive system. EQ-5D-3 L evaluates five domains (i.e., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with three levels of functioning (i.e., no problems, some problems or severe problems) and higher scores indicate a reduced QoL [28]. An internal medicine physician performed all of the questionnaires and measurements.

We set the follow-up period over 2 years, because it would be a sufficient timeframe to capture adverse outcomes like mortality, according to similar studies in literature [29, 30]. We ascertained deaths by a death certification search at March 2024, using the Hospital Information Management System (HIMS). The HIMS is an electronic software program used to process and manage the data of patients inside and beyond the hospital boundary.

### Statistical analysis

We presented the categorical variables as numbers and percentages and continuous variables as mean ± standard deviation or median (interquartile range; IQR) according to their distribution pattern. We checked the normality of continuous variables using histograms, probability plots, and the Kolmogorov-Smirnov test. We used Chi-square test with Yates correction, and Fisher's exact test where appropriate for the comparison of categorical variables. We used independent samples t-test or Mann-Whitney U test for the comparison of two independent groups, where necessary. We studied the overall concordance rate between different frailty scales with Spearman test and reported the correlation coefficients (r). We calculated overall survival in frailty defined by different scales with Kaplan–Meier log rank test. We defined follow-up duration as "the time (days) between date of death (for non-survivor participants) or March 2024 (for survivor participants) and date of the basal evaluation". We plotted Kaplan-Meier survival probability curves, marking specific points to indicate instances where the follow-up period concluded without observing mortality (i.e., censored points). We performed univariate and multivariate Cox regression analysis to find out whether frailty defined by alternative scales was predictor of mortality in follow-up. We defined four models for four different frailty scales in multivariate analyses and included confounding variables significantly associated with mortality in univariate analyses. We checked for multicollinearity before including parameters expected to have a strong correlation in the same regression models. We calculated hazard ratio (HR) and 95% CI and considered *p* values lower than 0.05 as statistical significance. We used the Statistical Package for the Social Sciences Statistics for Windows 26.0 program (SPSS Inc., Chicago, USA) for statistical analyses.

## Results

During the study period, there were 466 admissions to our center with a diagnosis of chronic HF. Among them, 263 patients had conditions that may prevent performing scales and measurements, 39 refused to participate in the study, and 63 could not be evaluated due to staffing issues during COVID-19 pandemic (Fig. 1). Finally, we included 101 older individuals with HF, 48 (42.8%) being female. The mean age was 75.8 ± 7.6. The number of outpatients and inpatients was balanced (50 vs. 51, for outpatients vs. inpatients). The majority of participants had HFpEF (81.8%) and the least had HFmrEF (8.0%). The median duration of HF diagnosis was 12 [8–15] years. Frailty prevalence was 63.4% with *SMFFS*, similar to *SOF* (65.3%). Prevalence was lowest with *EFS* (57.4%) and highest with *FRAIL* scale (71.3%). When we compared the study group according to their frailty status by *SMFFS*, frail participants were significantly older, had higher number of female participants and diuretic users, had lower EF and higher PAP, and had higher burden of geriatric syndromes (i.e., higher prevalence of sarcopenia, limitation(s) in ADL and IADL, falls in the previous year, and undernutrition). The detailed presentation of demographic and clinical characteristics and geriatric syndromes were given in Table 1.

We studied the correlation of *SMFFS* with the other commonly used frailty assessment tools. The median score for *SOF*, *FRAIL*, *EFS* were 1(0–1), 2 (1–3) and 5 (3–6), respectively at non-frail group according to *SMFFS*, whereas at frail group the median score were 2(2–3), 3(3–4) and 9(7–11). Accordingly, *SMFFS* demonstrated a strong correlation with other frailty tools, with *SOF* exhibiting the strongest correlation (correlation coefficients for *SOF*, *FRAIL*, and *EFS* were 0.794, 0.761, and 0.700, respectively). The correlation analyses of four frailty assessment tools can be found in Table 2.

After a median follow-up of 759 (489.5-831.5) days, 30 (29.7%) participants died. Mean survival time was significantly shorter in frail participants according to four frailty assessment tools [617.3 vs. 1272 days for *SMFFS* (log rank, $p < 0.001$), 746.8 vs. 1265.1 days for *FRAIL* (log rank, $p < 0.001$), 644.5 vs. 1218.1 days for *SOF* (log rank, $p = 0.001$), and 516.6 vs. 1193.6 days for *EFS* (log rank, $p < 0.001$] (Fig. 2).

Older age [HR = 1.08 (1.03–1.14), $p = 0.001$], cardiomegaly in echocardiography [HR = 4.2 (1.27–13.9), $p = 0.02$], higher PAP [HR = 1.05 (1.02–1.08); $p < 0.001$], falls in the previous year [HR = 2.47 (1.18–5.15), $p = 0.016$], limitation(s) in ADL [HR = 4.22 (1.97–9.06), $p < 0.001$], limitation(s) in IADL [HR = 5.09 (1.94–13.33), $p = 0.001$], undernutrition [HR = 5.26 (1.58–17.54), $p = 0.007$],

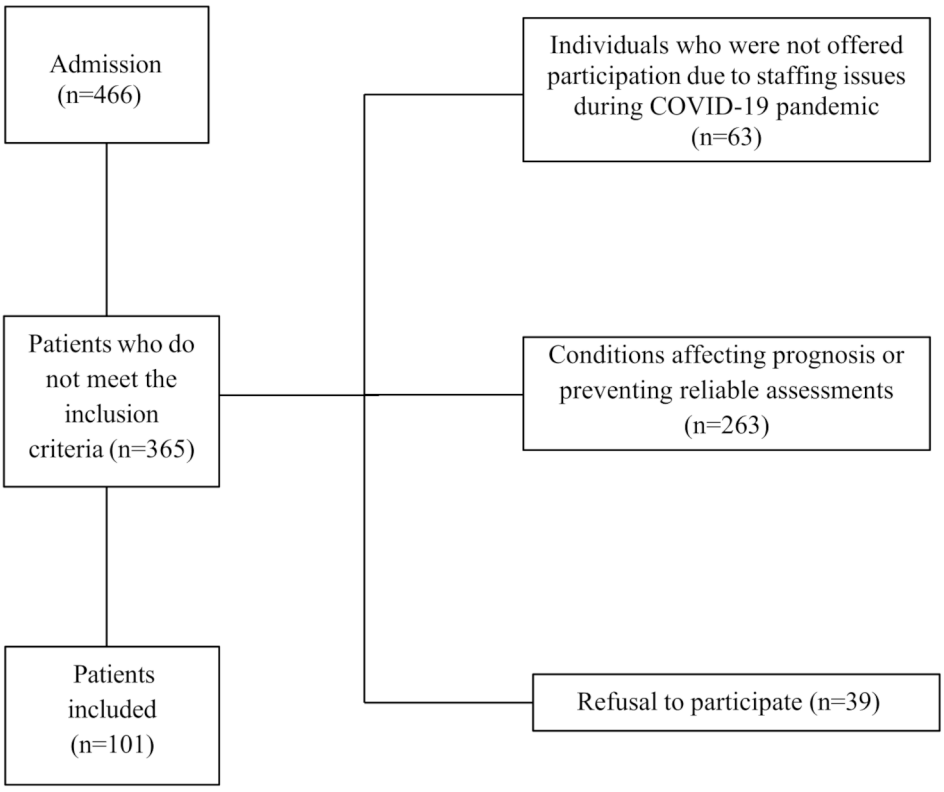


**Fig. 1** Flowchart on the number of patients included in the study

increased sarcopenia risk by SARC-F [HR = 18.22 (4.3-77.17), $p < 0.001$], probable sarcopenia [HR = 3.62 (1.69–7.75), $p = 0.001$], and poor QoL [HR = 1.40 (1.21–1.64), $p < 0.001$] were significantly associated with mortality in univariate analyses. Multivariate Cox regression analyses revealed that only cardiomegaly, high PAP and frailty according to *SMFFS* were independently associated with mortality in follow-up in older patients with HF [HR (95% CI) were 3.88 (1.05–14.3), 1.05 (1.01–1.09), and 10.96 (1.07–112.05), for cardiomegaly, higher PAP, and frailty by *SMFFS*, respectively] (Model 1) (Table 3). We created different models by replacing *SMFFS* with *SOF*, *EFS*, and *FRAIL*-defined frailty to find out whether other frailty tools were also capable of predicting mortality (Model 2–4). Accordingly, no frailty scale other than *SMFFS* was found to be successful in predicting all-cause mortality in older individuals with HF. Similar to the Model 1, only cardiomegaly and high PAP were independently associated with mortality in Model 2–4 (Table 3).

## Discussion

Recent guidelines recommend frailty assessment to be implemented into clinical practice of HF for risk stratification and treatment decisions [3, 4]. However, available frailty instruments are not always easy to apply in routine clinical practice and their validity needs to be elucidated. In this context, the *SMFFS* appears to be a scale that is practical and can be easily integrated into HF practice in different settings with being able to detect a significant number of frail individuals and predict mortality during follow-up.

The prevalence of frailty varies depending on the age group, frailty assessment method used, setting, and the classification and stage of HF. Frailty prevalence according to *SMFFS* was 63.4% in our study. Previously, the overall estimated frailty prevalence was reported to be 44.5% in patients with HF [6]. The fact that only older patients were included in our study and half of them were hospitalized may have caused the prevalence of frailty to be higher than reported. In previous studies, multidimensional frailty assessment has been reported to indicate more frail patients than only physical frailty assessments [6, 31]. On the contrary, in our study, a lower prevalence of frailty was detected with *EFS*, which provides a simplified frailty assessment of multiple domains. Nevertheless, *EFS* showed a strong correlation with *SMFFS* ($r = 0.700$, $p < 0.001$). The reason for the higher prevalence of frailty detected by physical frailty scales in our study population may be the overlapping physical characteristics of frailty and HF. Hemodynamic disturbances like congestion or reduced cardiac output and mitochondrial abnormalities hamper the oxygen utilization and exercise tolerance

**Table 1** Baseline characteristics of the participants according to their frailty status by the simpler modified Fried Frailty Scale

| | **Total (*n* = 101)** | **Not Frail (*n* = 37)** | **Frail (*n* = 64)** | ***p* value** |
|---|---|---|---|---|
| Age (mean ± SD) | 75.8 ± 7.6 | 72.7 ± 5.6 | 77.5 ± 8.1 | **0.001** |
| Female sex (*n*, %) | 48 (42.8) | 11 (29.7) | 37 (57.8) | **0.006** |
| Smoking status | | | | **0.032** |
| *Smoker* | 7 (6.9) | 4 (10.8) | 3 (4.7) | |
| *Ex-smoker* | 42 (41.6) | 19 (51.4) | 23 (35.9) | |
| *Not smoking* | 52 (51.5) | 14 (37.8) | 38 (59.4) | |
| Duration of CHF diagnosis (year) [med (IQR)] | 12 (8–15) | 12 (8-19.5) | 12 (8–15) | 0.412 |
| CCI [med (IQR)] | 6 (5–7) | 6 (4–7) | 6 (5–8) | 0.061 |
| Number of regular medications [med (IQR)] | 5 (4–6) | 5 (4–6) | 5 (4–6) | 0.925 |
| Regular medications (*n*, %) | | | | |
| *Beta-blockers* | 69 (68.3) | 26 (70.3) | 43 (67.2) | 0.748 |
| *RAAS inh* | 75 (74.3) | 28 (75.7) | 47 (73.4) | 0.804 |
| *MRA* | 18 (17.8) | 6 (16.2) | 12 (18.8) | 0.749 |
| *Diuretics (other than MRA)* | 78 (77.2) | 24 (64.9) | 54 (84.4) | **0.024** |
| *CCB* | 45 (44.6) | 14 (37.8) | 31 (48.4) | 0.302 |
| *Digitalis* | 6 (5.9) | 1 (2.7) | 5 (7.8) | 0.411 |
| Echocardiography findings | | | | |
| *Cardiomegaly (n, %)* | 61 (71.8) | 17 (63.0) | 44 (75.9) | 0.219 |
| *Hypokinesia/akinesia (n, %)* | 27 (30.7) | 11 (36.7) | 16 (27.6) | 0.381 |
| *Ventricular dilatation (n, %)* | 44 (51.8) | 11 (40.7) | 33 (56.9) | 0.165 |
| *LVEF (%) [med (IQR)]* | 60 (51.5–66) | 64 (56.5–68.5) | 59 (50–65) | **0.034** |
| *PAP (mmHg) [med (IQR)]* | 36 (25.75-45) | 30 (23-36.5) | 39 (30-48.5) | **0.002** |
| HF phenotypes | | | | 0.674 |
| *HFrEF* | 9 (10.2) | 2 (6.7) | 7 (12.1) | |
| *HFmrEF* | 7 (8.0) | 2 (6.7) | 5 (8.6) | |
| *HFpEF* | 72 (81.8) | 26 (86.7) | 46 (79.3) | |
| NT-ProBNP (pg/ml) [med (IQR)] | 1123.5 (306.25-4428.5) | 368 (121–1205) | 1868 (523-6193.5) | **< 0.001** |
| Hospitalization during the previous year (*n*, %) | 42 (41.6) | 11 (26.2) | 31 (73.8) | 0.066 |
| SARC-F score [med (IQR)] | 4 (2–6) | 1 (0–2) | 5 (4–7) | **< 0.001** |
| SARC-F (+) (%) | 54 (53.5) | 4 (10.8) | 50 (78.1) | **< 0.001** |
| HGS (kg) (mean ± SD) | | | | |
| *Female* | | 19.7 ± 4.5 | 14.4 ± 5.7 | **0.006** |
| *Male* | | 31.6 ± 5.2 | 21.9 ± 7.2 | **< 0.001** |
| Sarcopenia (*n*, %) | 43 (42.6) | 6 (16.2) | 37 (57.8) | **< 0.001** |
| Polypharmacy (*n*, %) | 67 (66.3) | 26 (70.3) | 41 (64.1) | 0.525 |
| ADL score [med (IQR)] | 6 (3.5-6) | 6 (6–6) | 5 (2–6) | **< 0.001** |
| Limitation in ADL (*n*, %) | 39 (38.6) | 5 (13.5) | 34 (53.1) | **0.045** |
| IADL score [med (IQR)] | 7 (3–8) | 8 (8–8) | 4 (2–7) | **< 0.001** |
| Limitation in IADL (*n*, %) | 56 (55.4) | 7 (18.9%) | 49 (76.6%) | **0.004** |
| Falls in the previous year (*n*, %) | 25 (24.8) | 3 (8.1) | 22 (34.4) | **0.004** |
| MNA-SF [med (IQR)] | 11 (7–12) | 13 (11–14) | 9 (6–11) | **< 0.001** |
| Undernutrition (*n*, %) | 70 (69.3) | 13 (35.1) | 57 (89.1) | **< 0.001** |
| EQ-5D [med (IQR)] | 9 (7–10) | 7 (6–9) | 10 (9–10) | **< 0.001** |

**Abbreviations**: SD (Standart Deriviation), med (Median), IQR (Inter Quartile Range), *n* (Number), % (Percentage), CHF (Chronic Heart Failure), CCI (Charlson Comorbidity Index), RAAS inh (Renin Angiotensin Activation System Inhibitor), MRA (Mineralocorticoid Receptor Antagonist), CCB (Calcium Channel Blocker), LVEF (Left Ventricular Ejection Fraction), PAP (Pulmonary Artery Pressure), HF (Heart Failure), HFrEF (HF with reduced Ejection Fraction), HFmrEF (HF with mildy reduced Ejection Fraction), HFpEF(HF with preserved Ejection Fraction), NT-proBNP (N-Terminal Pro-B-Type Natriuretic Peptide), HGS (Hand Grip Strength), ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living), MNA-SF (Mini Nutritional Assesment Short form), EQ-5D (Quality of Life)

Sarcopenia was defined as "probable" (i.e., HGS measurement lower than 27 kg and 16 kg for males and females, respectively) according to the EWGSOP2 consensus report

Limitation in ADL or IADL was defined as having at least one disability in any of the ADL or IADL domains

Undernutrition was defined as MNA-SF total score lower than 12 points

**Table 2** Correlation of simpler modified Fried Frailty Scale with different frailty screening tools

| | SMFFS | SOF | FRAIL | EFS |
|---|---|---|---|---|
| *SMFFS* | 1 | **0.794** | **0.761** | **0.700** |
| *SOF* | | 1 | **0.725** | 0.682 |
| *FRAIL* | | | 1 | 0.637 |
| *EFS* | | | | 1 |

Abbreviations: SMFFS (Simpler Modified Fried Frailty Scale), SOF (Study Of Osteoporotic Fracture Frailty İndex), EFS (Edmonton Frailty Scale)

r values showing strong correlation are given in bold. All of the correlations were statistically significant ($p < 0.001$ for all)

[32]. In addition, anorexia and weight loss are common during intervening acute episodes and contribute to the basal catabolic state caused by HF; accelerating the loss of muscle mass and functions [33, 34]. These characteristics in overall are expected to be more pronounced in hospitalized older adults with HF and more than half of the participants in our study are inpatients. Another possible reason of higher frailty prevalence in our study group is the high prevalence of HFpEF (81.8%). HFpEF was reported to be more associated with frailty compared to HFrEF and it is likely to be caused by the fact that patients with HFpEF suffer a higher burden of comorbidities and non-cardiac hospitalizations, which overall contribute to the development of frailty [2].

All frailty definitions were found to be associated with shortened survival in the Kaplan-Meier survival analysis. However, in the multivariate Cox regression analysis, only *SMFFS* was found to be independently associated with mortality among the frailty tests, in addition to the presence of cardiomegaly and increased PAP. The striking finding here is that there are objective and non-interpretive items in other scales (such as chair stand test in *SOF*, number of diseases in *FRAIL*, or TUG in *EFS*) and the

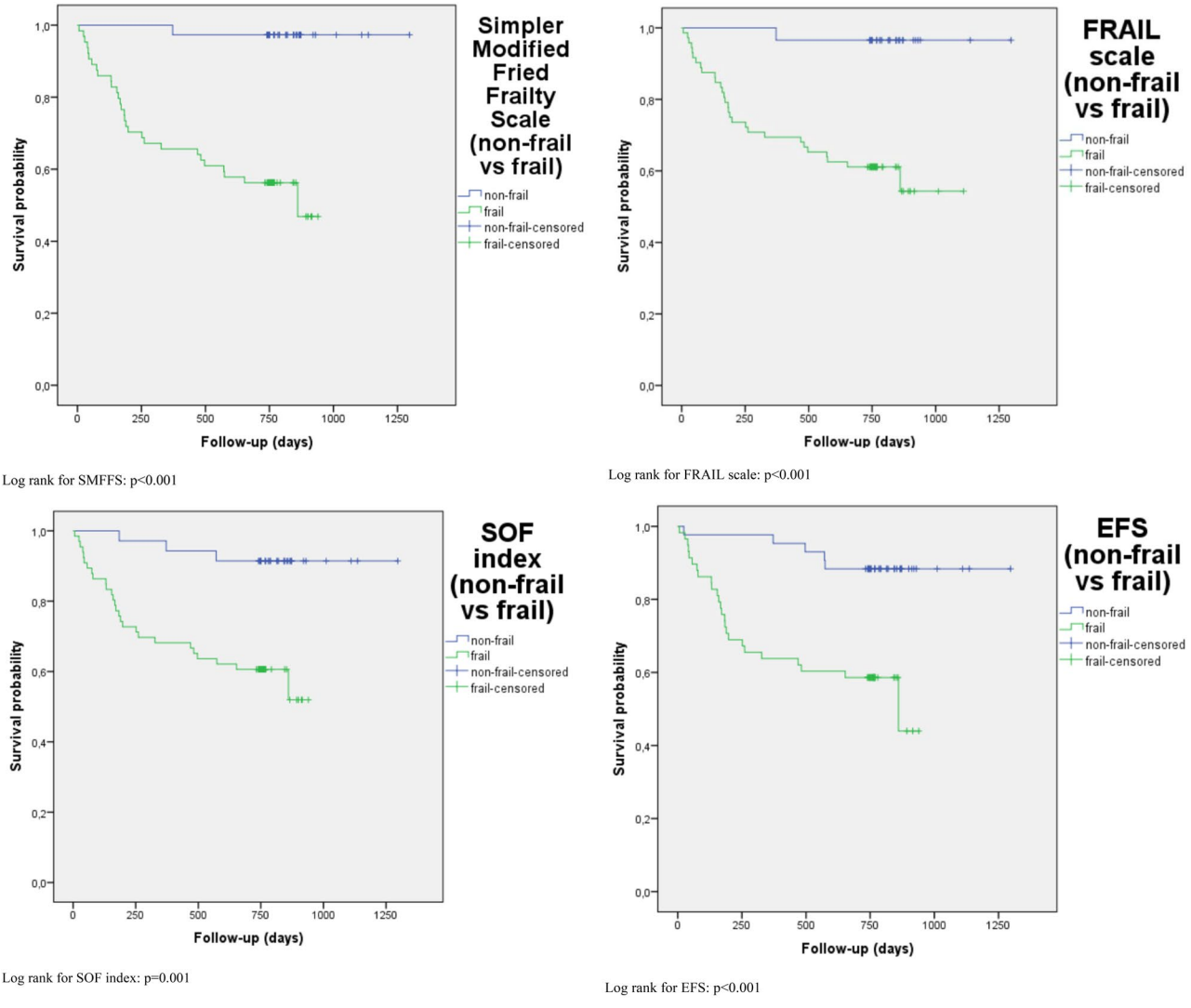


**Fig. 2** Kaplan-Meier survival analyses for the association of frailty with mortality in older adults with HF

**Table 3** Cox regression analyses for the independent associates of mortality in older patients with HF

| | Model 1 (SMFFS) | Model 2 (SOF) | Model 3 (EFS) | Model 4 (FRAIL) |
|---|---|---|---|---|
| *Age* | 1.03 (0.98–1.1), 0.237 | 1.03 (0.98–1.09), 0.260 | 1.03 (0.97–1.09), 0.296 | 1.03 (0.97–1.08), 0.367 |
| *Cardiomegaly* | **3.88 (1.05–14.3)**, **0.042** | **3.71 (1.01–13.68)**, **0.048** | **3.98 (1.20–14.44)**, **0.035** | **3.86 (1.06–14.14)**, **0.041** |
| *PAP* | **1.05 (1.01–1.09)**, **0.010** | **1.05 (1.01–1.09)**, **0.009** | **1.05 (1.01–1.08)**, **0.010** | **1.05 (1.01–1.08)**, **0.016** |
| *Falls in the previous year* | 1.69 (0.7–4.1), 0.247 | 1.55 (0.63–3.84), 0.339 | 1.62 (0.67–3.92), 0.283 | 1.75 (0.72–4.26), 0.220 |
| *Limitation in ADL* | 1.41 (0.39–5.09), 0.596 | 1.17 (0.36–3.76), 0.798 | 0.98 (0.30–3.22), 0.968 | 1.08 (0.33–3.51), 0.895 |
| *Limitation in IADL* | 0.42 (0.09–2.02), 0.279 | 0.86 (0.21–3.49), 0.861 | 0.84 (0.19–3.76), 0.822 | 1.06 (0.28–3.98), 0.932 |
| *Quality of life* | 1.27 (0.98–1.65), 0.068 | 1.24 (0.96–1.61), 0.104 | 1.24 (0.96–1.62), 0.103 | 1.23 (0.94–1.60), 0.126 |
| *Undernutrition* | 1.09 (0.25–4.78), 0.911 | 1.27 (0.29–5.56), 0.748 | 1.30 (0.30–5.61), 0.725 | 1.18 (0.27–5.15), 0.821 |
| *Sarcopenia* | 1.17 (0.42–3.28), 0.760 | 1.53 (0.56–4.18), 0.406 | 1.58 (0.57–4.39), 0.384 | 1.58 (0.56–4.44), 0.386 |
| *Frailty* | **10.96 (1.07–112.05)**, **0.044** | 2.37 (0.57–9.83), 0.235 | 2.05 (0.50–8.34), 0.317 | 2.05 (0.22–18.96), 0.527 |

Abbreviations: SMFFS (Simpler Modified Fried Frailty Scale), SOF (Study Of Osteoporotic Fracture Frailty İndex), EFS (Edmonton Frailty Scale), PAP (Pulmonary Artery Pressure), ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living)

Sarcopenia was defined as "probable" according to the EWGSOP2 consensus report

relationship with mortality is expected to be significant and high as well. However, only the association between mortality and *SMFFS*, which includes only subjective, self-reported items, is significant and *SMFFS*-defined frailty increases mortality by approximately 10 times during a median of 2-year follow-up. There are studies published over the years showing that self-reported health data should not be underestimated and is associated with mortality during follow-up in both patients with HF and the general older adult population [35–37]. In addition, it has been previously reported that *SMFFS* defined frailty predicts mortality in nursing home residents [11]. Furthermore, self-reported assessment of weakness, which is an important component of *SMFFS*, was also reported to be strongly correlated with objective muscle strength measurements and was also associated with mortality during follow-up [38, 39]. In light of this knowledge, the *SMFFS* appears to be a valid and useful tool in identifying older adults with HF at increased risk of mortality and intervenable factors to reduce their mortality risk (such as nutritional interventions for weight loss or protein supplementation and exercise programs for weakness, slow gait speed, and low physical activity).

Previous studies evaluating the relationship between physical frailty and mortality in patients with HF reported that the *FRAIL* and *SOF* scales are valid in predicting the risk of mortality [40, 41]. Although we also used the mentioned scales in addition to *SMFFS*, the same scales failed to predict mortality in this study. In fact, patients with HF are a very heterogeneous population: Classification and stage of HF, accompanying comorbidities, setting, sample size, and duration of follow-up are important determinants of the frailty-mortality relationship. Similar to ours, a Greek study using *SOF* and original *FFS* for frailty assessment reported that both frailty assessment methods failed to predict 90-days mortality in 193 older individuals with HFpEF and HFmrEF hospitalized with acute HF decompensation [42]. Although both studies included older patients hospitalized with acute decompensation who were frail and expected to be at high risk of mortality, a significant frailty-mortality relationship might be achieved with a longer follow-up period and a higher number of participants in both studies.

Some evidence suggests that multidimensional frailty instruments, rather than physical frailty scales, are more effective in risk stratification and are better predictors of mortality [43]. On the basis of HF, frailty has a more complex and intertwined pathophysiology and psychosocial determinants have also been reported to affect prognosis [44]. Therefore, optimum frailty assessment may indeed require more comprehensive approach in these patients. However, it is not yet clear how this comprehensive evaluation can be performed in the best and most practical way possible. In this context, Heart Failure Association (HFA) of the ESC published a consensus paper in 2019 proposing a foundation for the design of a tailored and validated score for frailty in HF [5]. Accordingly, they emphasized that frailty has multiple domains besides physical and they interact with each other, creating a dynamic state of increased vulnerability to stressors. For this reason, frailty assessment should not be limited to only physical frailty and that other frailty components such as psychocognitive and social domains should also be evaluated. However, available scales that provide multidimensional frailty assessment also have some important limitations in patients with HF: Most commonly known Frailty Index (FI) requires significant time and hampers its use in busy clinics [5]. In addition, it does not fully correspond to the concept of "a syndrome causing depleted reserves and resulting in increased vulnerability to stressors". Indeed, it works as a checklist and summarizes the presence of multiple diseases, their clinical and laboratory manifestations, and consequences into a composite index for risk prediction [45, 46]. The other commonly used *EFS* also examines multiple domains including cognition, social support, nutrition, and physical performance. However, it was reported to show a low sensitivity and risk of misclassification in patients with

chronic HF [47]. In line with this, the lowest prevalence of frailty was determined by *EFS* in our study and *EFS*-defined frailty was not significantly associated with mortality, after adjustment for confounding variables. Due to the limitations of available scales, HFA of the ESC position paper pioneered the development of an ideal scale which should be both easily applicable and addressing frailty in a holistic, multidimensional approach by evaluation of four domains together [physical (functional), psycho-cognitive, clinical and social]. They called this scale, which has not yet been developed, *the HFA frailty scale* [5]. Due to the impracticality of existing scales, it is common for clinicians to rely on their own judgements in treatment decisions (i.e., eyeball test or foot-of-the-bed assessment), but the validity of this approach is questionnable [48, 49]. In this context, our study shows that until an optimum and user-friendly scale is developed, *SMFFS* can be useful in assessment of frailty and prognosis in older patients with HF.

This study has certain limitations. First, although the study population includes older patients with HF, it is neither homogeneous enough to represent a single phenotype nor representative enough to be generalized to whole older adult population with HF diagnosis. Moreover, including New York Health Association (NYHA) classification might have provided additional insights regarding the HF-related functionality status of the patients. In fact, although NYHA classification is often used to assess functional status and to determine prognosis, its reliability in older adults is questionnable. It is highly affected from factors like frailty, disabilities, cognitive impairment, and psychiatric symptoms, frequently present in older adult population. Moreover, it was reported that differentiating between classes is highly subjective and agreement is not strong, even among board-certified cardiologists [50, 51]. Therefore, we assessed functionality of the patients from a more comprehensive geriatric perspective and chose to use the Katz and Lawton scales for this purpose.

Frailty assessment being limited to only baseline evaluation might be considered as another limitation; since frailty is a dynamic and can be a reversible condition and patients' frailty status may have varied during follow-up. However, we believe it is valuable to demonstrate that baseline frailty assessment by *SMFFS* can be useful to identify a vulnerable subgroup with an increased risk of mortality during follow-up. Although acknowledgment of CCI (as a measure of global comorbidity burden) and most geriatric syndromes in the study can be considered as an important strength, the absence of detailed information about other potential confounders such as specific chronic diseases or laboratory parameters can be accepted as another limitation. Frailty assessment through unintentional weight loss questioning may have been misleading; because fluctuating fluid status may have masked weight loss and increased false negative cases. In addition, since the *SMFFS* evaluates physical frailty, and functional limitations and decreased physical performance may be observed in patients with HF due to disease itself (floor effect), these patients may have been misclassified as frail. However, since it is very difficult to fully separate the intertwined HF-frailty concepts, it may at least be useful in distinguishing the group with high risk, whether due to frailty or HF.

Assessing the concordance of *SMFFS* with performance-based methods, such as the Short Physical Performance Battery (SPPB), which is recommended in clinical studies to define frail populations [52], could have provided more reliable results beyond the other scales used in the study. Since HF is a life-limiting disease and half of patients, especially in advanced stages, die within the first year [53], a median follow-up of 759 days may be considered a sufficient period and one of the strengths of our study. However, with a longer follow-up, the frailty-mortality relationship could probably be captured with other frailty scales too. Finally, the results should be interpreted with caution because sociocultural and educational differences may affect the results.

One of the strongest aspects of our study is that it is among the few studies evaluating the relationship between frailty and mortality during follow-up in older patients with HF. Another strength of the study is the use of the *SMFFS*, a simple, practical, and self-reported tool, applied for the first time in this specific patient population. Additionally, the study integrates other commonly used and validated frailty screening tools, further enhancing its robustness. Additionally, the frailty scales used in the study allowed for the assessment of frailty both unidimensionally (i.e., physical frailty alone) and multidimensionally (including physical, psycho-cognitive, and social dimensions). The follow-up period of the study is another strength, as it provides a sufficient duration to evaluate adverse outcomes such as HF-related mortality, compared to similar studies in the literature [29, 30].

## Conclusion

The SMFFS identified a significant number of frail patients among older adults with HF, demonstrated strong correlation with other commonly used frailty scales, and was predictive of mortality over a 2-year follow-up, even when adjusting for a list of confounding factors. The fact that it does not require measurements, relies solely on patient or caregiver reports, and is easy to administer makes it promising for seamless integration into practice of busy clinics. Large-scale future studies are needed to more clearly demonstrate its validity in

patients with HF across different stages and classes and to establish its association with other adverse outcomes.

## Supplementary Information

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Supplementary Material 1

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**Author contributions**
CK: writing review and editing, original draft preparation, formal analysis, software; SO: writing, review, original draft preparation, formal analysis ; GB: writing, review and editing; EBK: data curation, resources; MA: data curation, resources; AM: data curation, resources, investigation; MAK: conceptualization, methodology, supervision.

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**Data availability**
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## Declarations

**Ethics approval and consent to participate**
We obtained informed consent from all participants and performed the study according to the guidelines in the Helsinki Declaration. The local ethics committee (Istanbul University, Istanbul Medical Faculty Ethics Committee) approved the study (approval date/number: 2021/1508).

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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## Publisher's note