**Identiﬁcation of Frailty in Chronic Heart Failure**

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**Total word count: 4736 (including** the title page, abstract, text, references, tables, and figures legends)

Abstract

OBJECTIVES This study sought to report the prevalence of frailty, classiﬁcation performance, and agreement among 3 frailty assessment tools and 3 screening tools in chronic heart failure (CHF) patients.

BACKGROUND Frailty is common in patients with CHF. There are many available frailty tools, but no standard method for evaluating frailty.

METHODS We used the following frailty screening tools: the clinical frailty scale (CFS); the Derby frailty index; and the acute frailty network frailty criteria. We used the following frailty assessment tools: the Fried criteria; the Edmonton frailty score; and the Deﬁcit Index.

RESULTS A total of 467 consecutive ambulatory CHF patients (67% male; median age: 76 years; interquartile range [IQR]: 69 to 82 years; median N-terminal pro–B-type natriuretic peptide: 1,156 ng/l [IQR: 469 to 2,463 ng/l]) and 87 control patients (79% male; median age: 73 years (IQR: 69 to 77 years) were studied. The prevalence of frailty using the different tools was higher in CHF patients than in control patients (30% to 52% vs. 2% to 15%, respectively). Frail patients tended to be older, have worse symptoms, higher N-terminal pro–B-type natriuretic peptide levels, and more comorbidities. Of the screening tools, CFS had the strongest correlation and agreement with the assessment tools (correlation coefﬁcient: 0.86 to 0.89, kappa coefﬁcient: 0.65 to 0.72, depending on the frailty assessment tools, all p < 0.001). CFS had the highest sensitivity (87%) and speciﬁcity (89%) among screening tools and the lowest misclassiﬁcation rate (12%) among all 6 frailty tools in identifying frailty according to the standard combined frailty index.

CONCLUSIONS Frailty is common in CHF patients and is associated with increasing age, comorbidities, and severity of heart failure. CFS is a simple screening tool that identiﬁes a similar group using more lengthy assessment tools.

Key words: heart failure, frailty screening, assessment

**Introduction:**

Frailty is common in patients with chronic heart failure (CHF) and is associated with increased risk of death and hospitalisations.[[1]](#endnote-1),[[2]](#endnote-2),[[3]](#endnote-3) However, there is no standard method for evaluating frailty in patients with CHF.

Tools to evaluate frailty stem from two basic concepts of frailty – physical frailty and multi-dimensional frailty.

* The first was proposed by Fried and colleagues, who defined frailty as a physical syndrome using five criteria (Fried criteria): weak grip strength, unintentional weight loss, exhaustion, slow walking speed and low physical activity.[[4]](#endnote-4)
* The second concept was proposed by Rockwood et al who defined frailty as a state of vulnerability due to accumulation of health deficits. Frailty is measured by a deficit index which quantifies the cumulative burden of deficits. [[5]](#endnote-5),[[6]](#endnote-6)  The Edmonton frailty scale (EFS) is a simplified frailty assessment tool based on the concept of multi-dimensional frailty which has been shown to have good construct validity and reliability.[[7]](#endnote-7)

Despite their prognostic value and wide-spread use in research, the Fried criteria and the deficit index are not routinely used in clinical practice as they are time consuming to perform due to need of performing physical tests and evaluating multiple domains including co-morbidities, society situations, etc. Simple screening tools[[8]](#endnote-8) [[9]](#endnote-9) [[10]](#endnote-10) have been developed; they are much less time-consuming and easier to perform; hence might be a more feasible and cost-effective way of identifying at risk patients in busy clinical settings. However, but it is not clear whether they identify the same patients as the more comprehensive assessment tools. Very few studies have simultaneously evaluated different tools to quantify frailty in the same cohort of patients with CHF.[[11]](#endnote-11) To the best of our knowledge, no study has ever compared the performance of frailty screening tools versus assessment tools in patients with CHF. We therefore evaluated frailty in a cohort of patients with CHF using 3 commonly used frailty screening tools and 3 commonly used frailty assessment tools. We studied the prevalence of frailty, classification performance and agreement of these tools. We also compared the prevalence of frailty in patients with CHF against patients at risk of developing heart failure.

**Methods**

Study population

Consecutive ambulatory patients with CHF attending a community heart failure clinic were enrolled between September 2016 and March 2017. All patients had a pre-existing (>1 year) clinical diagnosis of CHF confirmed by either evidence of left ventricular systolic dysfunction on echocardiography (left ventricular ejection fraction (LVEF) <40% or at least moderate left ventricular systolic dysfunction by visual inspection if LVEF was not calculated), defined as heart failure with reduced ejection fraction, HeFREF; **or** normal left ventricular systolic function (LVEF >40% or better than, or equal to, mild-moderate left ventricular systolic dysfunction by visual inspection) and N-terminal pro-B-type natriuretic peptide (NTproBNP) >400 ng/L, defined as heart failure with normal ejection fraction, HeFNEF.[[12]](#endnote-12)

All patients had already been initiated on guideline-indicated treatment for heart failure and were regularly followed up.

Subjects who had previously consented to take part in research were recruited as controls. Control subjects were older than 65 years of age, with no previous or current symptoms or signs of HF and with normal left ventricular systolic function on echocardiography who also had risk factors for development of HF, including coronary artery disease, diabetes mellitus or hypertension.

During the visit, all patients had a full medical history, physical examination, blood tests (full blood count, urea and electrolytes and NTproBNP), an electrocardiogram and a consultation with a HF specialist.

Frailty screening and assessment

All patients and controls were screened and assessed by the same researcher (SS) for frailty (Appendix 1a)

The screening tools used were:

1. *The Derby frailty index* (DFI; scores as frail vs non-frail)

DFI is a quick pragmatic frailty identification tool initially developed in 2013.9 A patient is classified as frail if one of the following criteria is met: 1) ≥65 years old and a care home resident; 2) ≥75 years old with confusion, falls or reduced mobility; 3) ≥

85 years old with >4 co-morbidities.

1. *The acute frailty network criteria* (AFN; scores as frail vs non-frail)

AFN defines frailty as present in (a) people aged ≥85 years or (b) people aged ≥65 years with one or more of the following presenting features: cognitive impairment; resident in a care home; history of fragility fractures; Parkinson’s disease; recurrent falls.10

1. *The clinical frailty scale* (CFS; measures between 1 (very fit) and 9 (terminally ill))

Subjects are scored according to their functional capacity, level of dependence and co-morbidities. For example, a patient with uncontrolled symptoms who is not frankly dependent is classified as vulnerable and scores 4 on the CFS; while an individual with limited dependence on others for instrumental activities of daily living including finances, transportation, heavy housework and medications will be classified as mildly frail and scores 5 on the CFS. Subjects with a CFS >4 are classified as frail.8

The assessment tools used were:

1. *Fried frailty phenotype* (measures between 0 (normal) and 5 (very frail)):

The Fried Frailty phenotype4 is commonly used to validate other frailty criteria. Frailty is considered as a clinical syndrome based on five criteria: unintentional weight loss (≥10 lbs [≥4.5 kg] in the past year); self-reported exhaustion; weakness (low grip strength); slow walking speed (time to walk 5 meters ≥ 6-7 seconds depending on sex and height); and low physical activity (low weekly total energy expenditure assessed using the short version of the Minnesota Leisure Time Activity questionnaire[[13]](#endnote-13).) (Appendix 1b) Subjects with ≥ 3 points are classified as frail and those with 1-2 points and 0 points are classified as pre-frail and non-frail respectively.

1. *Edmonton frailty scale* (EFS; measures between 0-17)

EFS is a multi-dimensional frailty assessment tool which includes general health status, functional independence, social support, cognition, medication use, nutrition, continence and mood.7 EFS has been validated against the comprehensive geriatric assessment (CGA),[[14]](#endnote-14) a multi-dimensional, multidisciplinary diagnostic process used to determine medical, functional and psychosocial problems in elderly patients.7 Subjects with EFS 0-5 are classified as non-frail, those with EFS 6-7, 8-9, 10-11 and 12-17 are classified as vulnerable, mildly, moderately and severely frail respectively. Subjects with EFS ≥ 8 are classified as frail. (Appendix 1c)

1. *The Deficit Index* (DI; measures between 0.03-0.72)

Mitnitski and Rockwood consider frailty as a clinical state as a result of accumulation of deficits (symptoms, signs, co-morbidities and disabilities).[[15]](#endnote-15) These deficits are combined in a deficit index score to reflect the proportion of potential deficits present in a person.We selected 32 deficits according to previously published criteria6 to construct the deficit index. The first 14 items of the DI were related to activities of daily living which were collected by direct questioning of participants. The remaining items were based on information from patient’s medical records or physical tests during the visit. If a subject exhibited 5 out of the 32 possible deficits, the deficit index for that patient would be 5/32 or 0.16. We stratified patients and controls according to terciles of DI; those in the lower tercile were classified as non-frail while those in the middle and upper terciles were classified as pre-frail and frail respectively. (Appendix 1d)

Physical Tests:

1. Handgrip strength (HGS):

Hand grip strength was obtained with a handgrip dynamometer (Es-100 Ekj107, Evernew, Japan). The subject was seated with forearm resting on the arm of a chair and instructed to hold the dynamometer upright and squeeze as hard as possible. Three trials in the right hand followed by three trials in the left hand were recorded and the highest reading of the 6 was taken as the final reading.

1. Gait analysis
2. **Timed get up and go test:**

The area for the timed get up and go test was set up by measuring 3 meters from the front legs of a straight-backed armchair. The subject was instructed to: "Sit with your back against the chair and your arms on the arm rests. On the word `go,' stand upright, then walk at your normal pace to the line on the floor, turn around, return to the chair, and sit down." The time required to complete the test was time from the word `go' to time when the subject returned to the starting position. Subjects who took more than 10 seconds to complete the test were classified as frail. (Appendix 1c)

1. **Five metre walk test:**

The subject was instructed to walk at a normal pace for 5 meters according to their ability. The time required to complete the test was time from the word `go' to time when the subject reached the 5-meter-point. Subjects who took more than 6-7 seconds (depending on sex and height) to complete the test were classified as frail. (Appendix 1b)

Co-morbidities

Co-morbidities were measured using the Charlson co-morbidity index/score.[[16]](#endnote-16) Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or a previous clinical diagnosis.[[17]](#endnote-17) Current haemoglobin (Hb) levels were used to define anaemia (Hb <13.0 g/dL in men and <12.0 g/dL in women).[[18]](#endnote-18) Diabetes mellitus was defined according to the guideline from Diabetes UK.[[19]](#endnote-19) Patients consented to the use of electronic medical records to identify previous clinical history of myocardial infarction, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), dementia, rheumatological disease, peptic ulcer, hemiplegia/ paraplegia, liver or renal disease or malignancy.

Statistical analysis

Continuous data are expressed as a median with interquartile range (IQR) (25th to 75th centiles) and categorical data are expressed as n (%). Independent t tests and Mann-Whitney U tests were used to compare two continuous variables for normally and non-normally distributed data. The chi-squared test was used to compare proportions between groups. Pearson’s correlation or Spearman’s correlation coefficients were used to assess the relationships between two variables. Venn diagrams were used to illustrate the relationship between screening and assessment tools. Kappa statistics were used to study the agreement between frailty screening tools and assessment tools.

Since there is no gold standard in evaluating frailty in patients with CHF, for each of the frailty tools, we used the results of the *other* 5 tools to produce a single combined frailty index which we assumed to be the gold standard frailty tool. This methodology has been previously suggested by Pablo et al.[[20]](#endnote-20) Similarly, for each of the physical tests (timed get up and go test, 5 metre walk test and hand grip strength), we used the results of the 5 frailty tools which do not include the physical test, to produce a single combined frailty index as the gold standard frailty tool. Subjects were defined as frail if so identified by at least 3 of the 5 tools. The sensitivity, specificity and predictive values for each of the individual tools and physical tests in identifying frailty according to the combined index were calculated.

To investigate the bias associated with CFS being a subjective frailty screening tool, in addition to the principal investigator (SS), a second investigator (JW) also completed the CFS for a random sample of 23 patients. Kappa statistics were used to determine the inter-operator agreement.

All statistical analyses were performed using SPSS 22 (SPSS INc.,Chicago, IL, USA) and The Stata (14th Version, StataCorp, TX, USA) statistical computer package. A two-tailed P-value of <0.05 was considered significant in all analyses.

The study conformed to the principles outlined in the Declaration of Helsinki and was approved by relevant ethical bodies. All subjects gave their written informed consent for their data to be used for research.

**Results**

A total of 467 consecutive patients with CHF and 87 controls was studied. Table 1a shows the baseline characteristics of the HF cohort vs controls. The majority of patients and controls were male and elderly; 17% of those with CHF were older than 85 years (vs 2% of controls). Most of the patients with CHF had HeFREF (62%) with a median NTproBNP of over 1100ng/L; around one fifth had severe symptoms (NYHA III/IV).

**Prevalence of frailty**

The prevalence of frailty varied according to frailty tools used. It was much more common in patients than in controls, regardless of the frailty tool used (HF: 30-52% vs controls: 2-15%). (Table 2)

Amongst the frailty assessment tools, the Fried criteria scored the greatest proportion of patients as frail (52%) while EFS scored the lowest proportion as frail (30%) (Figure 1). 26% (N=119) of patients were classified as frail by **all** 3 assessment tools. (Central illustration)

Amongst the frailty screening tools, DFI scored the greatest proportion of patients as frail (48%) while CFS scored the lowest proportion as frail (44%) (Figure 1). 27% (N=128) of patients were classified as frail by **all** 3 screening tools. (Central illustration)

The prevalence of frailty was higher in patients with HeFNEF than HeFREF. (Table 3) The prevalence of frailty was higher in patients with atrial fibrillation (AF) than in those in sinus rhythm. The prevalence of frailty increased with decreasing BMI and increasing NYHA class, age and NTproBNP.

**Prevalence of pre-frailty**

The prevalence of pre-frailty varied greatly depending on the assessment tool used. (Table 2) According to the EFS, the prevalence of pre-frailty was much higher in patients than controls, but according to the Fried criteria, pre-frailty was as common in both groups.

The Fried criteria scored the greatest proportion of patients as pre-frail (32%) while the EFS scored the lowest proportion as pre-frail (19%). (Figure 1) Only 3% (N=13) of patients were classified as ‘pre-frail’ by **all** 3 assessment tools (Appendix 2)

**Relationship between frailty and clinical data**

Compared to those who are not frail, frail patients were older, had worse symptoms, higher NTproBNP, worse renal function and anaemia. They were more likely to be on diuretics but less likely to be on ACE-inhibitors, beta-blockers and mineralocorticoid antagonist; they also had a lower BMI and more co-morbidities: especially dementia, COPD, depression, recurrent falls and incontinence. (Table 1b)

Compared to those who were classified as frail by 1 or 2 assessment tools, patients who were classified as frail by all 3 assessment tools were older, had worse symptoms, more severe heart failure, lower haemoglobin level and higher comorbidity burden. (Appendix 3 – we can add the table in rebuttal letter to appendix if the editor is in agreement).

**Relationship between different frailty tools**

The relationship between the results of the frailty scores is shown in Table 4. Of the 3 frailty *screening* tools, CFS had the strongest correlation with the frailty *assessment* tools (correlation coefficient: 0.86-0.89, depending on the frailty assessment tools, all P<0.001)

**Detection of frailty: screening tools vs assessment tools**

Of the screening tools, CFS had the highest and DFI the lowest agreement with the assessment tools in distinguishing between frail and non-frail patients. (Table 5)

**Frailty tools *vs* combined index**

Table 6 shows the sensitivity, specificity and misclassification rates of different frailty tools (screening vs assessment vs single physical tests) in identifying frailty according to the combined index (the presumed gold standard for identifying frailty).

Of the screening tools, CFS had the highest sensitivity (87%) and specificity (89%). DFI had the highest false positive rate (16%) and false negative rate (10%). CFS had the lowest misclassification rate (12%).

Of the assessment tools, the Fried criteria had the highest sensitivity (93%) and EFS had the highest specificity (98%). The Fried criteria had the highest false positive rate (14%) and EFS has the highest false negative rate (18%).

Of the three single physical tests, timed get up and go test had the highest sensitivity (97%) and 5m walk test had the highest specificity (59%). Grip strength had the highest false positive rate (25%) and false negative rate (3%). Overall, timed get up and go test had the lowest misclassification rate (25%).

Compared to frailty assessments or screening tools, single physical tests have higher overall sensitivities but lower specificities and higher misclassification rates.

**Inter-operator agreement of CFS:**

There was close agreement between the two operators’ judgements on degree of frailty in a random sample of subjects (N=23) using the CFS, with a Kappa coefficient (K) of 0.72 (95% CI: 0.51-0.93, p<0.001).

**Time needed to complete frailty screening vs assessment:**

Frailty screening on average takes no more than 1 minute to complete, whereas frailty assessment on average takes 15 minutes to complete, depending on the mobility of patients.

**Discussion**

We found that frailty is very common amongst outpatients with CHF, but that the prevalence varied from 30 to 52% depending on the assessment tool used. Our findings are similar to those from a meta-analysis involving 5522 ambulatory patients with CHF or older adults aged 70 to 79 years. Frailty was assessed by several tools including the Fried criteria, comprehensive geriatric assessment, the deficit index, frailty staging system, modified frailty scale and the Health ABC Short Physical Performance Battery (HABC battery) and Gill index. The prevalence of frailty was between 18 and 54% depending on the population studied.[[21]](#endnote-21) There was substantial variance in prevalence of frailty in the meta-analysis probably due to heterogeneity of populations studied. Our results are a more accurate reflection of the true prevalence of frailty in patients with CHF as we evaluated frailty using 6 different scoring tools in the same cohort of patients.

Frailty was more common in patients with HeFNEF than in patients with HeFREF. The patients with HeFNEF were older and had a greater burden of non-cardiac co-morbidities, themselves associated with reduced functional status and increased risk of hospitalisation.[[22]](#endnote-22),[[23]](#endnote-23) AF becomes more common with age, and is particularly common in patients with HeFNEF. It is itself associated with the development and progression of frailty.[[24]](#endnote-24)

Ours is the first paper to compare simple frailty screening tools with more comprehensive assessment tools in patients with CHF. Whilst we found that there was substantial overlap between patients identified as frail by each tool, the overlap was not very great. Although we found a correlation between frailty screening and assessment tools, the relation was modest for some, suggesting that the tools are measuring differing aspects of a common phenotype, and that none is on its own definitive.

The different tools have strengths and weaknesses. The Fried criteria objectively measure physical functioning, but other domains, particularly cognition, are not considered. The DI covers multiple domains including physical functioning and co-morbidities, and is thus a more comprehensive tool than the Fried criteria. The EFS, similar to DI, also examines multiple domains including cognition, social support, medication, nutrition and mood; it also includes straightforward physical performance measures (timed get up and go test). Frailty assessments require significant time to perform (on average 10-15 minutes depending on the mobility of patients), which is not ideal in busy clinical settings.

Screening tools are much easier to use. They do not require physical measurements to be carried out and can be completed within a minute. Amongst the screening tools, CFS has the highest sensitivity and specificity with the lowest misclassification rate. We found that CFS, was as effective as lengthy frailty assessments in detecting frailty, and it is therefore appealing for use in clinical practice. CFS has a subjective component, but we found inter-operator agreement to be good.

Worsening results on physical performance measures such as grip strength and walking speed predict increasing mortality and risk of institutionalisation.[[25]](#endnote-25),[[26]](#endnote-26) We found that single physical tests have higher sensitivities but lower specificities than frailty assessment or screening tools, and higher misclassification rates. Further studies will clarify whether single physical measures or simple frailty screening tools have comparable prognostic value to more comprehensive frailty assessments.

**Study limitations**

Firstly, because this is a single-centre study conducted in the UK with limited sample size, external validation of our results from other populations with different healthcare and social systems is needed. Our study is, however, the largest study which directly compares several commonly used frailty screening and assessment tools in consecutive, unselected, patients with CHF.

Secondly, we have only studied 6 of the most commonly used frailty tools in literature. A large number of frailty screening and assessment tools has been proposed and identified patients at risk of adverse outcome in other clinical scenarios.[[27]](#endnote-27)

Thirdly, this study only focuses on reporting prevalence of frailty by the different tools, but we have not evaluated the predictive role of these tools.

Fourthly, we only included patients with a diagnosis of dementia if they had capacity in the investigator’s opinion to consent for the study. We are therefore unable to report on frailty in patients with dementia so severe as to be considered lacking in capacity.

**Conclusion**

Frailty is common in patients with CHF. CFS is a short and easy to use frailty screening tool, which has comparable effectiveness to lengthy frailty assessments in identifying frailty. CFS should therefore be considered when assessing patients with CHF to enable identification of at-risk individuals. Further work is required to study the prognostic value of simple screening vs assessment tools in patients with CHF.

**Perspectives:**

**Competency in medical knowledge 1**: Frailty is common in patients with CHF, with a prevalence of 30 -52% depending on the screening or assessment tool used.

**Competency in medical knowledge 2**: Frailty is associated with increasing age, co-morbidities and severity of HF.

**Competency in medical knowledge 3**: CFS is a short and easy to use frailty screening tool which has comparable effectiveness to lengthy frailty assessments in identifying frailty in patients with CHF. CFS should be considered when assessing patients with CHF.

**Translational outlook**: Recognition of the high prevalence of frailty in patients with CHF should stimulate further research on the prognostic value of simple screening vs assessment tools.

**Acknowledgement: None**

**Funding: None**

**Conflict of interest: None**

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