ESC HEART FAILURE
ESC Heart Failure 2018; **5**: 949–953
Published online 12 June 2018 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12300

SHORT COMMUNICATION

Prospective assessment of combined handgrip strength and Mini-Cog identifies hospitalized heart failure patients at increased post-hospitalization risk

Emer Joyce[1], Erik H. Howell[3], Alpana Senapati[4], Randall C. Starling[1] and Eiran Z. Gorodeski[1,2]*

[1]*Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Desk J3-4, 9500 Euclid Ave., Cleveland, OH 44195, USA;* [2]*Center for Connected Care, Cleveland Clinic, Cleveland, OH, USA;* [3]*Department of Medicine, University of Rochester Medical Center, Rochester, NY, USA;* [4]*Houston Methodist DeBakey Heart and Vascular Center, Houston, TX, USA*

Abstract

Aims The utility of combined assessment of both frailty and cognitive impairment in hospitalized heart failure (HF) patients for incremental post-discharge risk stratification, using handgrip strength and Mini-Cog as feasible representative parameters, was investigated.

Methods and results A prospective, single-centre cohort study of older adults (age ≥65) hospitalized for HF being discharged to home was performed. Pre-discharge, grip strength was assessed using a dynamometer (Jamar hydrolic hand dynamometer, Lafayette Instruments, Lafayette, IN, USA) and was defined as weak if the maximal value was below the gender-derived and body mass index-derived cut-offs according to Fried criteria. Cognition was assessed using the Mini-Cog. The presence of impairment was defined as a score of <2. Outcome measures were all-cause readmission or emergency department visit (primary) or all-cause mortality (secondary) at 6 months. A total of 56 patients (mean age 77 ± 7 years, 73% male) were enrolled. The majority (n = 33, 59%) had weak grip strength, either with (n = 5) or without (n = 28) cognitive impairment. The highest risk for both readmission and mortality occurred in those with weak grip strength and cognitive impairment in combination (log-rank $P < 0.0001$ and $P = 0.01$, respectively).

Conclusions Patients who are frail by grip strength assessment and cognitively impaired according to severely reduced Mini-Cog performance show the worst midterm post-discharge outcomes after HF hospitalization.

Keywords Frailty; Cognitive impairment; Hospitalized heart failure; Grip strength; Readmission

Received: 5 October 2017; Revised: 25 March 2018; Accepted: 16 April 2018
**Correspondence to: Eiran Z. Gorodeski, MD, MPH, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Desk J3-4, 9500 Euclid Ave., Cleveland, OH 44195, USA. Email: gorodee@ccf.org*

Introduction

Frailty, a pathobiological syndrome characterized by heightened vulnerability to stressors and diminished physiological reserves,[1] is increasingly recognized in heart failure (HF) patients. The presence of frailty has been consistently associated with worse outcomes across the spectrum of HF, including in hospitalized HF patients.[2,3] While traditionally assessed by the multi-component Fried scale,[1] handgrip strength is a highly feasible single-item measure of frailty particularly suited to hospitalized and immobile HF patients and has already been studied and related to prognosis in the advanced HF population.[4,5]

Cognitive impairment is also highly prevalent in HF patients[6] and has similarly demonstrated a negative effect on outcomes including survival and readmission risk in patients hospitalized with HF.[7] The Mini-Cog measure is a validated, practical tool for assessment of cognitive impairment in routine clinical practice, which predicts higher post-hospitalization risk.[7] Despite the prevalence and frequent coexistence[8] of these novel clinical biomarkers in similar populations, no studies to date have investigated the prognostic value of assessing both parameters in hospitalized HF patients. We hypothesized that those patients who have both frailty and cognitive impairment will have the worst outcomes. Therefore, the aim of this study was to determine the

combined utility of cognitive function and frailty, using handgrip strength and Mini-Cog as feasible representative parameters, for incremental post-hospitalization risk stratification.

Methods

This was a single-centre prospective cohort study of older adults (age ≥65 years) hospitalized for a primary diagnosis of HF, intended to discharge to home. Details of this cohort including inclusion and exclusion criteria have been published elsewhere.[9] Recruitment and study procedures were carried out by two internal medicine resident physicians who are also co-authors of this work (E. H. H. and A. S.). Study participants were identified from a daily hospital admission list that was cross-verified by the inclusion criteria.[9] Recruitment was carried out in intermittent 1 week blocks between November 2012 and March 2013. During these blocks, all patients were reviewed, approached, and if agreeable to participate, were required to sign informed consent in a consecutive manner. The study was approved by the Institutional Review Board at Cleveland Clinic and complies with the World Medical Association's Declaration of Helsinki.

Prior to hospital discharge, cognition was assessed using the Mini-Cog measure, a three-item recall and clock-drawing test.[7] Patients were scored on a 5-point scale (1 point for each correct word recalled and 2 points for correct clock drawing) with a score of <2 defined as indicating a high likelihood of cognitive impairment.[10] A cut-off score of <2 is more specific but less sensitive in identifying cognitive impairment. Grip strength was assessed using a dynamometer (Jamar hydrolic hand dynamometer, Lafayette Instruments, Lafayette, IN, USA) and performed in the dominant hand three times. Patients were classified as having weak grip strength if their maximal value obtained was below the gender-derived and body mass index-derived cut-offs according to the Fried criteria.[1]

Primary outcome measure investigated was freedom from a composite of all-cause readmission or emergency department visit up to 6 months. Freedom from all-cause mortality at 6 months was assessed as a secondary outcome.

Continuous variables are presented as mean and standard deviation. Categorical variables are presented as frequencies and percentages. Patients were stratified into groups based on the presence or the absence of cognitive impairment and/or weak grip strength. Clinical characteristics were compared across groups using Pearson's chi-squared test for categorical variables and the Wilcoxon or Kruskal–Wallis test for continuous variables. Survival free from clinical endpoints is presented as Kaplan–Meier time-to-event plots and compared across groups using the log-rank test. All analyses were performed with R version 3.3.1.

Results

Of a total of 94 consecutive hospitalized HF patients reviewed for enrolment during the study period, 56 (mean age 77 ± 7 years, 73% male, 32% preserved ejection fraction) met criteria for inclusion. The majority of the cohort (n = 33, 59%) had weak grip strength with or without cognitive impairment by the predefined standard definitions (weak grip strength/cognitive impairment absent, n = 28; weak grip strength/cognitive impairment present, n = 5). No patient had cognitive impairment in the absence of weak grip strength. *Table 1* illustrates baseline demographic and clinical characteristics according to stratified groups. Patients who had both weak grip strength and cognitive impairment showed trends towards having more acute kidney injury during hospitalization and more baseline co-morbidities (chronic obstructive lung disease and liver disease) than the other groups as well as being significantly more likely to have a history of cancer (P = 0.03).

Overall at 6 months post-hospitalization, 29 patients were readmitted or presented to the emergency department, and six patients died. The majority of adverse events for both endpoints occurred in those with weak grip strength with or without cognitive impairment (70% and 100% for primary and secondary endpoints, respectively). On Kaplan–Meier analysis, the highest risk for the primary outcome of time to first hospital readmission or emergency department visit occurred in those with both weak grip strength and cognitive impairment, intermediate risk occurred in those with weak grip strength but no cognitive impairment, and least risk was seen in those without either adverse clinical biomarker (log-rank $P < 0.0001$) (*Figure 1*). Similar results were seen for risk of all-cause mortality at 6 months (log-rank P = 0.01) (*Figure 2*).

Discussion

Frailty assessment in hospitalized HF patients has been shown to define risk otherwise uncaptured by traditional risk scores.[2,5] Given the impracticality of multi-element scales, interest is growing in single-item measures such as handgrip strength, which can be feasibly administered by the bedside and do not require the patient to be ambulatory but still provide similar risk stratification. In an advanced HF population, weak grip strength, detected in 22% of the population, was associated with worse clinical outcomes after left ventricular assist device implantation.[4] Much less is known about the prevalence of weak grip strength in an all-comer, older adult, hospitalized HF population. This study adds to the current body of literature by demonstrating that the majority of patients (60%) in this predominantly elderly male study cohort met the criteria

Table 1 Demographic and clinical characteristics according to categories of Mini-Cog performance and handgrip strength

	Strong grip strength/ cognitive impairment absent (n = 23)	Weak grip strength/ cognitive impairment absent (n = 28)	Weak grip strength/ cognitive impairment present (n = 5)	P-value
Age (years) (range)	75 (67–90)	77 (66–92)	80 (69–88)	0.41
Male	14 (61)	23 (82)	4 (80)	0.22
Black race	8 (35)	7 (25)	3 (60)	0.28
Length of stay (days)	12 (9)	10 (5)	9 (4)	0.91
Body mass index (kg/m^2)	27 (5)	29 (6)	28 (4)	0.93
Ischaemic cardiomyopathy	7 (30)	12 (43)	1 (20)	0.49
HFpEF	7 (30)	9 (32)	2 (40)	0.92
NYHA III or IV	5 (22)	13 (46)	2 (40)	0.18
Pacemaker or defibrillator	6 (26)	12 (43)	3 (60)	0.26
Atrial fibrillation or flutter	16 (70)	18 (64)	3 (60)	0.88
Medications				
ACE-inhibitor	7 (30)	9 (32)	1 (20)	0.86
ARB	6 (26)	5 (18)	0 (0)	0.39
Aldosterone antagonist	5 (22)	10 (36)	1 (20)	0.49
Beta-blocker	16 (70)	24 (86)	4 (80)	0.38
CCB	6 (26)	6 (21)	1 (20)	0.91
Diuretic	16 (70)	26 (93)	4 (80)	0.10
Hydralazine	2 (9)	4 (18)	2 (40)	0.21
Nitrate	4 (17)	6 (21)	1 (20)	0.94
Digoxin	3 (13)	2 (7)	1 (20)	0.62
Peripheral arterial disease	8 (35)	7 (25)	1 (20)	0.67
≥2 alcoholic drinks weekly	4 (17)	3 (11)	0 (0)	0.52
Diabetes mellitus	12 (52)	12 (43)	3 (60)	0.69
Hypertension	20 (87)	23 (82)	4 (80)	0.87
Stroke				0.65
No history of stroke	20 (87)	21 (75)	4 (80)	
Recovered without disability	3 (13)	5 (18)	1 (20)	
Persistent disability	0 (0)	2 (7)	0 (0)	
Chronic kidney disease	8 (35)	17 (61)	1 (20)	0.32
Acute kidney injury	6 (26)	12 (43)	4 (80)	0.07
COPD	3 (13)	7 (25)	3 (60)	0.08
Liver disease	1 (4)	0 (0)	1 (20)	0.08
History of malignancy	10 (43)	6 (21)	4 (80)	0.03
Laboratory testing				
Haemoglobin	11 (2.1)	11 (2.1)	9.1 (1.1)	0.09
Haematocrit	35 (6)	35 (6)	29 (3)	0.17
Creatinine	1.8 (1.2)	1.8 (1.1)	2.1 (0.7)	0.42
Blood urea nitrogen	37 (22)	45 (34)	46 (19)	0.51
Albumin	3.3 (0.4)	3.4 (0.4)	3.0 (0.3)	0.15

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; HFpEF, heart failure with preserved ejection fraction; NYHA, New York Heart Association.
All categorical variables were shown as number and per cent, and all continuous variables were shown as mean and standard deviation, unless noted otherwise.

as defined by Fried for the 'weakness' component of the classic frailty phenotype.

Cognitive impairment is also gaining increasing recognition as a clinical biomarker of worse post-discharge outcomes in patients hospitalized for HF. Cognitive impairment as defined by a conservative Mini-Cog cut-off of <2 was present in 9% of the cohort. Cognitive dysfunction is not routinely assessed alongside frailty measures, despite growing recognition of the coexistence of both of these adverse substrates in elderly patients, including HF populations.[8,11,12] Boyle *et al*.[11] found that physical frailty predicts the development of mild cognitive impairment in 750 retirement community dwellers without cognitive dysfunction at baseline. In the French Three-City Study that enrolled over 6000 community-dwelling older adults, cognitive impairment was present in 22% of the frail patients and improved the predictive validity of the frailty phenotype for adverse outcomes.[12]

Despite studies such as these highlighting the etiological associations between the two conditions, the potential clinical impact of the presence of both of these adverse factors in hospitalized HF patients is largely unknown. In the advanced HF population, Jha *et al*.[13] recently determined that the combination of both physical frailty (assessed by modified Fried scale) and cognitive impairment (as assessed by the Montreal Cognitive Assessment) best identified patients referred for heart transplantation with the highest risk for early death. In the present study, frail patients identified by weak grip strength demonstrated significantly worse

Figure 1 Freedom from readmission or emergency department visit at 6 months.

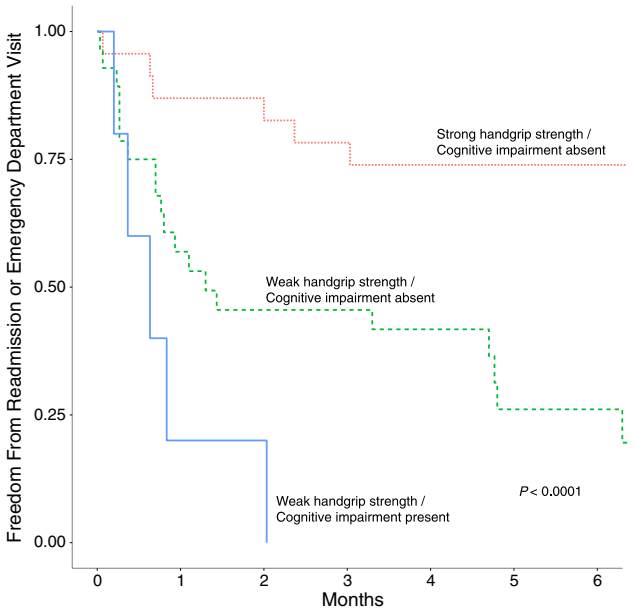
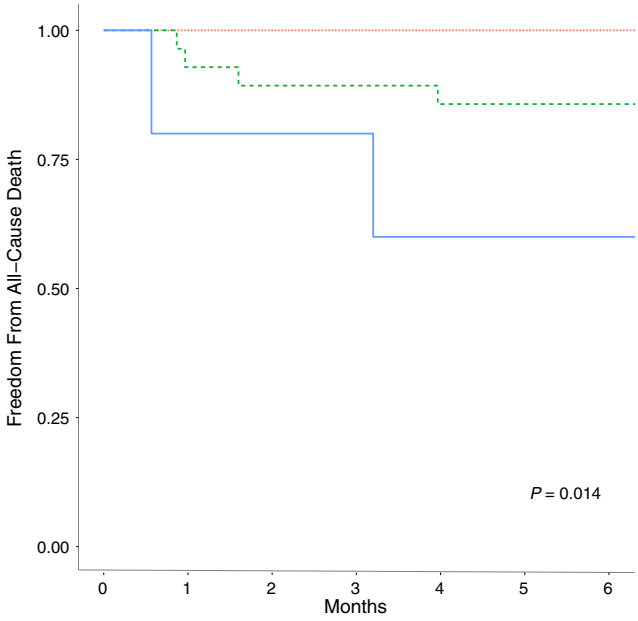


Figure 2 Freedom from all-cause mortality at 6 months.



6 month post-hospitalization risk (both readmission and survival) compared with those with normal grip strength. The combination of having both weak grip strength and cognitive impairment was associated with the highest risk of requiring readmission or emergency department visit by 6 months post-discharge. In addition, these patients showed significantly worse 6 month survival. It is important to note that the burden of multi-morbidity was also high in weak and cognitively impaired patients, consistent with previously published literature describing a tight correlation between burden of co-morbidity and chronic HF.[14] However, it is also known that being frail is not synonymous with the presence of chronic diseases alone.[1] Determining the exact mechanisms by which the presence of both markers in combination identifies those patients with the worst outcomes is outside the scope of this study but is likely related to the significant pathobiological overlap between the combined domains of HF, vascular disease, other co-morbidities, and ageing.

This study has several limitations. Study numbers were modest, leading to limited numbers in subgroups of frailty categories. However, this was a prospective study with a well-phenotyped cohort and importantly was based on systematic generation of clinical data. Frailty is a multi-domain syndrome and may be under-represented by a single measure such as grip strength. Gait speed has been associated with survival in chronic HF patients[15] and warrants testing as an alternative single-item marker for frailty alongside Mini-Cog in future investigations in this population. The Mini-Cog test is a screening tool rather than a diagnostic one, and its generalizability may be limited given that there are multiple other screening tools for cognitive impairment currently in use with a lack of consensus about which one should be used in HF patients.[16] However, previous studies have shown that it is highly valid in detecting cognitive impairment and dementia.[17] The present study was not adequately powered to detect definitive differences between subgroups in terms of outcome measures. Larger, multicentre prospective studies are needed to determine the incremental predictive ability of this combined "Grip–Cog" measurement for post-hospitalization risk stratification.

In summary, in this prospective cohort study of older adults hospitalized for HF, the known independently adverse phenotypes of frailty and cognitive impairment are prevalent, frequently coexist, and when present in combination, identify patients at worst post-hospitalization risk. Earlier detection of the presence of both of these simply administered novel clinical biomarkers may highlight the need for targeted intervention in order to improve short-term and longer-term outcomes in elderly HF populations.

Conflict of interest

None declared.

Funding

This work was supported by The Hunnell Fund.

References

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**: M146–M156.
2. Chaudhry SI, McAvay G, Chen S, Whitson H, Newman AB, Krumholz HM, Gill TM. Risk factors for hospital admission among older persons with newly diagnosed heart failure: findings from the Cardiovascular Health Study. *J Am Coll Cardiol* 2013; **61**: 635–642.
3. Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, Popma JJ, Ferrucci L, Forman DE. Frailty assessment in the cardiovascular care of older adults. *J Am Coll Cardiol* 2014; **63**: 747–762.
4. Chung CJ, Wu C, Jones M, Kato TS, Dam TT, Givens RC, Templeton DL, Maurer MS, Naka Y, Takayama H, Mancini DM, Schulze PC. Reduced handgrip strength as a marker of frailty predicts clinical outcomes in patients with heart failure undergoing ventricular assist device placement. *J Card Fail* 2014; **20**: 310–315.
5. Joyce E. Frailty in advanced heart failure. *Heart Fail Clin* 2016; **12**: 363–374.
6. Dodson JA, Truong TT, Towle VR, Kerins G, Chaudhry SI. Cognitive impairment in older adults with heart failure: prevalence, documentation, and impact on outcomes. *Am J Med* 2013; **126**: 120–126.
7. Patel A, Parikh R, Howell EH, Hsich E, Landers SH, Gorodeski EZ. Mini-cog performance: novel marker of post discharge risk among patients hospitalized for heart failure. *Circ Heart Fail* 2015; **8**: 8–16.
8. Butts B, Gary R. Coexisting frailty, cognitive impairment, and heart failure: implications for clinical care. *J Clin Outcomes Manag* 2015; **22**: 38–46.
9. Howell EH, Senapati A, Hsich E, Gorodeski EZ. Medication self-management skills and cognitive impairment in older adults hospitalized for heart failure: a cross-sectional study. *SAGE Open Medicine* 2017; **5**: 1–10.
10. Borson S, Scanlan JM, Watanabe J, Tu SP, Lessig M. Simplifying detection of cognitive impairment: comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. *J Am Geriatr Soc* 2005; **53**: 871–874.
11. Boyle PA, Buchman AS, Wilson RS, Leurgans SE, Bennett DA. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. *J Am Geriatr Soc* 2010; **58**: 248–255.
12. Avila-Funes JA, Amieva H, Barberger-Gateau P, Le Goff M, Raoux N, Ritchie K, Carriere I, Tavernier B, Tzourio C, Gutierrez-Robledo LM, Dartigues JF. Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. *J Am Geriatr Soc* 2009; **57**: 453–461.
13. Jha SR, Hannu MK, Gore K, Chang S, Newton P, Wilhelm K, Hayward CS, Jabbour A, Kotlyar E, Keogh A, Dhital K, Granger E, Jansz P, Spratt PM, Montgomery E, Harkess M, Tunicliff P, Davidson PM, Macdonald PS. Cognitive impairment improves the predictive validity of physical frailty for mortality in patients with advanced heart failure referred for heart transplantation. *J Heart Lung Transplant* 2016; **35**: 1092–1100.
14. Chamberlain AM, St Sauver JL, Gerber Y, Manemann SM, Boyd CM, Dunlay SM, Rocca WA, Finney Rutten LJ, Jiang R, Weston SA, Roger VL. Multimorbidity in heart failure: a community perspective. *Am J Med* 2015; **128**: 38–45.
15. Pulignano G, Del Sindaco D, Di Lenarda A, Alunni G, Senni M, Tarantini L, Cioffi G, Tinti MD, Barbati G, Minardi G, Uguccioni M. Incremental value of gait speed in predicting prognosis of older adults with heart failure: insights from the IMAGE-HF study. *JACC Heart Fail* 2016; **4**: 289–298.
16. Davis KK, Allen JK. Identifying cognitive impairment in heart failure: a review of screening measures. *Heart Lung* 2013; **42**: 92–97.
17. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. *J Am Geriatr Soc* 2003; **51**: 1451–1454.