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Comparison of Frequency of Frailty and Severely Impaired Physical Function in Patients 60 Years Hospitalized with Acute Decompensated Heart Failure vs Chronic Stable Heart Failure With Reduced and Preserved Left Ventricular Ejection Fraction

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Abstract

Older patients with acute decompensated heart failure (ADHF) have persistently poor outcomes including frequent rehospitalization despite guidelines based therapy. We hypothesized that such patients have multiple, severe impairments in physical function, cognition, and mood that are not addressed by current care pathways. We prospectively examined frailty, physical function, cognition, mood and quality of life in 27 consecutive older ADHF patients at 3 medical centers and compared these to 197 participants in 3 age-matched cohorts: stable heart failure with preserved ejection fraction (n=80); stable heart failure with reduced ejection fraction (n=56) and healthy older adults (n=61). Based on Fried criteria, frailty was present in 56% of ADHF patients vs. 0 for the age-matched chronic heart failure and health cohorts. ADHF patients had markedly reduced Short Physical Performance Battery score (5.3 ± 2.8) and six-minute walk distance (178 ± 102 meters) ($p < 0.001$ vs other cohorts), with severe deficits in all domains of physical function: balance, mobility, strength and endurance. In the ADHF patients, cognitive impairment

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(78%) and depression (30%) were common, and quality of life was poor. In conclusion, older ADHF patients are frequently frail with severe and widespread impairments in physical function, cognition, mood and quality of life that may contribute to their persistently poor outcomes, are frequently unrecognized, are not addressed in current ADHF care paradigms, and are potentially modifiable with targeted interventions.

Keywords

Heart failure; frailty; physical function; aging

Introduction

Following a hospitalization for acute decompensated heart failure (ADHF) older patients have high rates of morbidity, including frequent rehospitalization, mortality, and health care expenditures, and these remain high even with adherence to guidelines-based heart failure (HF)-specific management strategies.¹ Importantly, these patients typically have multiple comorbidities and subsequent adverse events are frequently due to non-cardiac causes.² The development of ADHF and the physiologic stressors associated with the hospital environment may accelerate functional decline and frailty already present due to aging, chronic HF, and multimorbidity, exacerbate impairments in cognition and mood, and lead to further declines in quality of life.³ These impairments are associated with poor outcomes and may be modifiable with targeted interventions.^{3,4} However, current ADHF management strategies rarely address frailty and associated impairments in physical function, cognition or mood.³ A comprehensive examination of these impairments could help guide investigations of novel assessments and interventions for older patients with ADHF. The purpose of this prospective study was to comprehensively assess impairments in older patients hospitalized with ADHF using standardized assessments of frailty, physical function, cognition, mood and quality of life and compare key measures of physical function and frailty to age-matched cohorts of stable HF patients and healthy older adults.

Methods

We conducted a prospective, comprehensive, multi-dimensional assessment of 27 patients 60 years hospitalized with ADHF and compared their performance in key measures to 3 age-matched cohorts previously enrolled as outpatients: 1) stable HF with preserved ejection fraction (HFpEF) (n=80);⁵ 2) stable HF with reduced ejection fraction (HFrEF) (n=56);⁶ and 3) healthy older adults (n=61).⁷

The ADHF cohort was recruited at 3 academic medical centers (Wake Forest Medical, Duke University and Thomas Jefferson University). The diagnosis of ADHF was based on pre-specified criteria (symptoms, signs, clinical tests and response to medical therapy) and confirmed by a study HF cardiologist. Participants had to have been independent with basic activities of daily living prior to hospitalization and ambulatory (assistive device allowed) with discharge planned to home at the time of enrollment.

As previously described, chronic, stable HF patients with either preserved⁵ (≥ 50%) or reduced⁶ (< 35%) left ventricular ejection fraction were recruited from Wake Forest Medical Center using the validated Rich et al. and National Health and Nutrition Examination Survey HF criteria.^{8,9} These participants had no recent hospitalizations or medical condition that could mimic HF.

The age-matched healthy cohort was recruited from the community, excluding those with any chronic medical illness or chronic medication prescription.⁷ All participants provided informed consent and the study was approved by the Institutional Review Boards at each center.

Trained personnel using standardized protocols performed all study measures. In the ADHF cohort, assessments were collected during hospitalization after successful initial treatment for ADHF and an average of 1 day prior to hospital discharge. Identical measures were collected in the age-matched chronic, stable HFpEF patients and healthy older adults at pre-scheduled study visits. Assessment in the chronic stable HFrEF cohort was limited to 6-minute walk distance (6MWD).

Frailty was based on meeting at least 3 of 5 previously validated cut-offs for the domains described by Fried and colleagues: slowness, weakness, weight loss, exhaustion, and low physical activity.¹⁰⁻¹² Additional definitions of this key outcome included: Short Physical Performance Battery (SPPB) score <6, gait speed <0.8 m/s and handgrip strength <30 kg in men and <20 kg in women.¹²

Physical function was assessed by 6MWD, the SPPB, and handgrip strength. The 6MWD was collected in an unobstructed corridor according to recommended guidelines.¹³ The SPPB includes 3 components, standing balance, gait speed over 4 meters, and time to complete repeated chair rise. Each component is scored from 0-4 and summed for a total score of 0-12.¹⁴ Handgrip strength was based on the better of 2 measures in the dominant (stronger) hand using a hand dynamometer with the participant seated and elbow flexed to 90 degrees.¹⁵ Cognitive function and depression were assessed using the Montreal Cognitive Assessment and the 15-item Geriatric Depression Scale, respectively.^{16,17} The Kansas City Cardiomyopathy Questionnaire was used to assess quality of life.¹⁸ Medical history, including clinical history of depression or cognitive impairment, and demographic information were obtained through chart review and patient interview.

Continuous variables are reported as mean ± standard deviation (SD) or median and interquartile range, and categorical variables as number and percentage. Comparisons between age-matched cohorts were made using Fisher's exact test for categorical variables and analysis of covariance for continuous variables, adjusting for age and ejection fraction and with Bonferroni correction for multiple comparisons when appropriate. Among ADHF patients, comparisons of measures between HFrEF and HFpEF were made by an independent samples t-test for continuous variables and by Fisher's exact test for categorical variables. A two-tailed p value of < 0.05 was required for significance.

Results

Participant age was similar across all cohorts (Table 1). Women were more common in HFpEF (80%) and less common in HFrEF (34%) compared to the ADHF (59%), which included a mix of patients with HFpEF and HFrEF, and healthy cohorts (62%) ($p<0.05$ for each comparison). The ADHF cohort was more racially diverse (Table 1).

Frailty was common ($>50\%$) in ADHF participants by multiple criteria but was rare or absent in other cohorts (0% to 14% depending on the cohort and criteria applied) (Table 2).

Older patients with ADHF had severe reductions in all domains of physical function: balance, mobility (gait speed), strength and endurance (Table 2; Figures 1 and 2). Average 6MWD, SPPB score, and gait speed were approximately 50% lower in ADHF than in stable HF or healthy older adults. Balance deficits were unexpectedly common, with the majority of ADHF participants unable to attempt (33%) or maintain (56%) tandem stance for even 3 seconds (normal is 10 seconds). Lower extremity strength (chair rise performance) was especially impaired, with 41% of ADHF participants lacking the leg strength to stand from a seated position without the use of arms even once. Weakness appeared generalized as handgrip strength was also significantly reduced in ADHF. Functional impairments in chronic stable HF cohorts were less severe and less generalized than in ADHF but were greater than in healthy age-matched participants. Thus, there was a steep gradient of impairments from healthy older adults to chronic HF to ADHF.

Even after initial treatment for ADHF, hospitalized patients had much greater symptom burden and severely diminished functional status (Kansas City Cardiomyopathy Questionnaire score 44 ± 18 in ADHF vs 60 ± 17 in chronic stable HFpEF; $p=0.006$).

In ADHF patients, the mean (SD) Montreal Cognitive Assessment score was low (20.6 ± 4.8) and mild cognitive impairment (score ≤ 25) was very frequent (78%). Thirty percent of ADHF participants had depression based on a Geriatric Depression Scale score ≥ 6 . Of note, no ADHF participant had a clinical diagnosis of dementia or delirium, and only 11% had a history of depression, suggesting significant under-recognition.

When ADHF patients were divided by ejection fraction ($\geq 45\%$; $n=11$ vs $<45\%$; $n=16$), patient characteristics and all study measures were similar ($p>0.2$).

Discussion

We conducted a prospective, comprehensive, multi-dimensional assessment of older patients hospitalized with ADHF, including frailty, multiple domains of physical function, cognition, mood and quality of life. We compared frailty and physical function measures to age-matched cohorts of chronic stable HF patients and healthy adults ≥ 60 years old. Such multidimensional assessments have not previously been described in older ADHF patients in a detailed, comprehensive fashion and compared with multiple appropriate age-matched control cohorts. We found that older patients hospitalized with ADHF have high rates of frailty ($\geq 50\%$), profound impairments in physical function across all domains (balance, mobility, strength and endurance), frequent cognitive impairment and depressive symptoms,

and poor quality of life. Collectively, these findings support our hypothesis that older patients with ADHF have widespread deficits strongly associated with adverse outcomes.^{4,12,19}

Impairments in physical function, a key determinant of frailty status by most measures, were surprisingly broad and severe in older ADHF patients. A particularly novel and important finding of our study was that there were severe impairments in balance and mobility, which were not present in the chronic stable HFpEF cohort. Severe lower extremity weakness rendered approximately 40% of older ADHF patients unable to rise from a chair even once without assistance or use of upper extremities. All individuals in the non-ADHF groups could rise from a chair at least 5 consecutive times. The profoundly reduced 6MWD (178 meters) is comparable to ambulatory patients with advanced HF awaiting left ventricular assist device implantation (204 m).²⁰

A combination of factors likely contribute to the severe impairments in physical function, including pre-existing impairments from chronic HF, aging, and comorbid disease, the systemic effects of ADHF mediated through activation of inflammatory and neurohumoral pathways, and hospital-associated immobility. Skeletal muscle in patients with ADHF may be particularly susceptible to these acute insults. During chronic stable HF, both HFrEF and HFpEF have multiple severe abnormalities in skeletal muscle composition and function that contribute to their physical dysfunction.²¹ In addition, acute illness has been associated with a myopathic process that progresses rapidly soon after hospitalization.²² Hospital-associated immobility likely further compounds muscle loss and physical deconditioning, with older hospitalized patients spending <5% of their time ambulating and >80% lying in bed.²³ This degree of immobility is promoted by hospital processes and is often unrecognized by clinicians.^{3,23}

Impairment in ADHF was not limited to physical function. Cognitive impairment (78%) and depressed mood (30%) were also common in ADHF patients and frequently unrecognized clinically. The high rate of cognitive impairment in ADHF (75-80%) is consistent with other studies²⁴ as is the finding that cognitive impairment is generally unrecognized clinically.^{24,25} Cognition impairment and depressed mood have implications for HF self-care²⁴ and have been associated with increased risk of adverse events including mortality and rehospitalization.^{19,25} Abnormalities in cognition and mood have also been associated with physical impairments commonly used to describe frailty, raising the consideration that they may share common biologic mechanisms,²⁶ and underscoring the systemic, multi-organ nature of impairments in older patients with ADHF, increasing susceptibility to frailty and vulnerability to adverse clinical events.^{4,11}

Our findings have clear clinical implications. These impairments may contribute to the persistently high rate of adverse outcomes in older patients after acute HF hospitalization, including frequent rehospitalizations and falls with delayed, incomplete recovery, which has been termed the “post-hospital syndrome”,³ and the fact that a majority of subsequent clinical outcomes in older HF patients are for non-cardiac causes.²⁷ However, current management guidelines for ADHF do not usually acknowledge these deficits, care models

do not address them, and our findings support that they are often unrecognized or unaddressed in clinical practice.

Our findings also suggest a potential role for targeted, individualized physical function interventions in older ADHF patients. However, little is known about the safety and efficacy of traditional cardiac rehabilitation (CR) / exercise training in patients recovering from an ADHF hospitalization. Studies establishing the benefit of CR in chronic, stable HF patients systematically excluded patients with recent ADHF such that patients within 6 weeks of an ADHF episode are excluded from reimbursement for CR services by the Centers for Medicare and Medicaid Services.²⁸ Furthermore, CR in its conventional form may not adequately address the needs of this older, frail population with severe and widespread functional impairments. Indeed, multiple reports suggest that initiating traditional walking-based exercise interventions in frail older persons, who frequently have balance and mobility deficits such as we observed, leads to excess adverse events, falls, and injuries.^{29,30}

These new insights may support the development of novel intervention strategies to address these deficits and thereby improve functional status, quality of life and clinical outcomes, and potentially reduced health care costs in the growing population of older patients with ADHF. Based on these findings, we developed a novel rehabilitation intervention to address the severe physical function deficits in older patients with ADHF, which is currently being tested in a recently launched, multicenter NIH-funded clinical trial: A Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF) ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02196038) Identifier: NCT02196038).

There are some limitations to this study. The cohort of older ADHF patients was relatively small, but generalizability is supported by enrollment from 3 sites. Measures in the stable HFrEF cohort were more limited than other groups, but among the ADHF cohort there was no difference in any study measure between HFrEF and HFpEF, and our findings were unchanged after adjusting for ejection fraction. We were unable to adjust for all differences in study cohorts (e.g. gender, race) that could have contributed to the differences in study measures. However, the large magnitude of impairments observed in ADHF patients is unlikely to be explained by these differences alone. We cannot exclude that intergroup differences in frequency of beta-blocker medications may have influenced our results. However, beta-blockers would not be expected to have large effect on the SPPB or 6MWD. This study focused on functional status near the time of hospital discharge and does not include pre-hospitalization assessments or post-hospitalization follow-up. Longitudinal studies could help to further clarify acute vs chronic impairments as well as to confirm key prognostic measures.

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Figure 1.

Comparison of 6MWD among study cohorts. 6MWD (mean ± SE) was significantly less in ADHF (178 ± 20 meters) compared to each of the age-matched cohorts (HFpEF (417 ± 9 meters), HFrEF (432 ± 16 meters), and Healthy (563 ± 9 meters)) (p-value <0.001 for all comparisons with ADHF). Stable HFpEF and stable HFrEF were similar (p=1.0).

Comparisons made adjusting for age and ejection fraction and using Bonferroni correction for multiple comparisons. Abbreviations: 6MWD = 6-minute walk distance; ADHF = acute decompensated heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

Figure 2.

Comparison of SPPB among study cohorts. Total SPPB score and each component score (chair rise, gait speed, balance) (mean $\pm$ SE) was significantly less in ADHF (5.3 ± 0.5 units) than either Stable HFpEF (9.6 ± 0.2 units) or Healthy (11.3 ± 0.1 units) (p-value <0.001 for all comparisons with ADHF). Comparisons made adjusting for age and ejection fraction and using Bonferroni correction for multiple comparisons. Abbreviations: ADHF = acute decompensated heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection; SPPB = Short Physical Performance Battery.

Table 1

Participant Characteristics by Cohort

Characteristics	ADHF (N=27)	Stable HFpEF (N=80)	Stable HFREF (N=56)	Healthy (N=61)
Age (years)	72 ± 10	71 ± 7	69 ± 5	69 ± 7
Women	59% [†]	80%	34%	62%
Black	56% [*]	29%	18%	5%
Body mass index (kg/m ²)	29.3±6.7 [*]	31.9±6.5	26.6±4.3	25.9±4.9
Left ventricular ejection fraction (%)	37±16 [*]	62±7	32±10	66±7
Hypertension	89% [*]	88%	52%	N/A
Diabetes mellitus	48% [§]	23%	27%	N/A
Ischemic heart disease	63% [†]	0%	25%	N/A
Diuretic	100% [†]	73%	82%	N/A
Beta-blocker	85% [†]	31%	11%	N/A
Angiotensin-converting-enzyme inhibitor or Angiotensin II receptor blocker	59%	53%	79%	N/A
Digoxin	7% [‡]	1%	71%	N/A

Data presented as mean ± SD or percentage.

Abbreviations: ADHF = acute decompensated heart failure; HFpEF = heart failure with preserved ejection fraction; HFREF = heart failure with reduced ejection fraction; N/A = non-applicable

^{*} ADHF is significantly different from all 3 groups

[†] ADHF is significantly different than HFREF and HFPEF

[‡] ADHF is significantly different than HFREF

[§] ADHF is significantly different than HFPEF. Comparisons made using analysis of variance for continuous variables and Fisher's exact test for categorical variables.

Table 2**Frailty and Physical Function**

	ADHF	Stable HFpEF	Healthy	ADHF vs HFpEF; p-value	ADHF vs Healthy; p-value
Frailty Phenotype					
Frail (3 of 5 domains met)	56%	0	0	<0.001	<0.001
Pre-frail (1-2 domains met)	41%	58%	10%	0.30	<0.001
Frailty domains					
Slowness (gait speed)	74%	4%	0	<0.001	<0.001
Weakness (handgrip)	56%	11%	8%	<0.001	<0.001
Weight loss	0	0	2%	1.0	1.0
Exhaustion	85%	33%	0	<0.001	<0.001
Low physical activity	33%	25%	0	0.84	<0.001
Additional Frailty Criteria					
Short Physical Performance Battery score < 6	56%	0	0	<0.001	<0.001
Gait speed < 0.8 m/s	81%	14%	0	<0.001	<0.001
Handgrip strength men <30 kg; women <20 kg	48%	9%	3%	<0.001	<0.001
Physical Function					
Short Physical Performance Battery components					
Chair rise score	0.7 ± 0.7	2.2 ± 0.9 [*]	3.3 ± 0.7	< 0.01	< 0.01
Balance score	2.4 ± 1.4	3.7 ± 0.6	4.0 ± 0.2	< 0.01	< 0.01
Gait speed score	2.0 ± 1.2	3.7 ± 0.5	4.0 ± 0.0	< 0.01	< 0.01
Gait speed (m/s)	0.58 ± 0.23	0.98 ± 0.21 [*]	1.22 ± 0.17	< 0.01	< 0.01
Handgrip strength (kg)					
Men	30.3 ± 11.3	46.1 ± 8.0	52.4 ± 10.3	< 0.01	< 0.01
Women	20.7 ± 6.1	28.9 ± 9.4	27.6 ± 6.9	< 0.01	< 0.04

Abbreviations: ADHF = acute decompensated heart failure; HFpEF = heart failure with preserved ejection fraction

^{*} Chronic, stable HFpEF significantly different compared to Healthy ($p \pm 0.01$). Data presented as mean ± standard deviation or percentage. For continuous variables, P-value is from analysis of covariance, with age and ejection fraction as covariates. For categorical variables, P-value is from Fisher's exact test. Bonferroni correction used for multiple comparisons.