## Frequency of and Significance of Physical Frailty in Patients With Heart Failure



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Physical frailty is an important prognostic indicator in heart failure (HF); however, few studies have examined the relation between physical frailty and invasive hemodynamics among adults with HF. The purpose of this study was to characterize physical frailty in HF in relation to invasive hemodynamics. We enrolled 49 patients with New York Heart Association class II to IV HF when participants were scheduled for a right-sided cardiac heart catheterization procedure. Physical frailty was measured according to the "frailty phenotype": shrinking, weakness, slowness, physical exhaustion, and low physical activity. Markers of invasive hemodynamics were derived from a formal review of right-sided cardiac catheterization tracings, and projected survival was calculated using the Seattle HF model. The mean age of the sample (n = 49) was  $57.4 \pm 9.7$  years, 67% were men, 92% had New York Heart Association class III/IV HF, and 67% had nonischemic HF. Physical frailty was identified in 24 participants (49%) and was associated with worse Seattle HF model 1-year projected survival (p = 0.007). After adjusting for projected survival, physically frail participants had lower cardiac index (by both thermodilution and the Fick equation) and higher heart rates compared with those not physically frail (all p <0.05). In conclusion, physical frailty is highly prevalent in patients with HF and is associated with low-output HF. © 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;119:1243-1249)

Heart failure (HF) is an increasingly common condition with  $\sim 915,000$  new cases diagnosed every year. The rising numbers of adults with HF coupled with the complexity of clinical management<sup>2</sup> highlight the need to pursue new lines of inquiry in HF. Frailty is a highly prevalent condition generally among older adults<sup>3</sup> and specifically among those with cardiovascular disease.<sup>4,5</sup> A number of studies have demonstrated high prevalence rates of frailty in HF and worse associated clinical outcomes among frail adults with HF.<sup>6-10</sup> Following recommendations by several HF groups to include a frailty assessment in HF,<sup>11,12</sup> there is a critical need to study all aspects of "physical" frailty in HF, including the relation between physical frailty and other commonly used markers in HF, such as invasive hemodynamics. The purpose of this study was to characterize physical frailty in HF by quantifying differences in invasive hemodynamics between physically frail and nonphysically frail patients with HF.

### Methods

This article addresses a primary aim of a US National Institutes of Health-funded cross-sectional study that involved comprehensive measurements of physical frailty

and invasive hemodynamics in HF. The study was conducted between July 2015 and March 2016. After initial screening and approval by the HF cardiologists, potential participants who met the inclusion criteria were approached when scheduled for a clinically indicated right-sided cardiac catheterization (RHC) procedure (Figure 1). Physical frailty criteria were assessed usually on the same day as, or within 7 days of, the RHC procedure.

The sampling frame for this study was adult women and men with HF who receive care from an HF practice (outpatient clinic and/or inpatient facilities) at an academic medical center in the Pacific Northwest and required a RHC procedure during the study period. Formal inclusion criteria included age  $\geq 21$  years, ability to read and comprehend fifth-grade English, New York Heart Association (NYHA) functional class II to IV (i.e., current HF symptoms), and those who underwent RHC for clinical purposes. Participants were excluded if they had previously had a heart transplant or ventricular assist device, had major and uncorrected hearing dysfunction, or were otherwise unable to complete the requirements of the study (e.g., life-threatening illness). This study was approved by the university institutional review board, and written informed consent was obtained from all participants.

Data on age, gender, and race were obtained using a sociodemographic questionnaire. Functional status (i.e., NYHA) was assessed and documented by an attending HF cardiologist. Data on history, duration, etiology, and treatment of HF along with clinical characteristics were collected through an in-depth review of the electronic medical record. Co-morbid conditions were summarized using the Charlson Comorbidity Index.<sup>14</sup>

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See page 1248 for disclosure information.

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# Enrollment Screened for eligibility (n = 64) Excluded (n = 14) Not meeting inclusion criteria (n = 2) Declined to participate (n = 5) Did not respond (n = 7) Enrolled (n = 50) Survey not returned (reason: did not want to complete; n = 1) Analysis (n = 49)

Figure 1. Enrollment flow diagram for symptom biology and accelerated aging in Heart Failure Study. We screened 64 adults for our study, 50 adults were enrolled, and 49 adults were analyzed.

All RHC procedures were performed without the use of sedation by either advanced HF cardiologists or interventional cardiologists. After completion of the RHC procedure, we reviewed the RHC tracings and reports. We collected data and calculated pressures based on waveforms, including right atrial pressure, pulmonary artery pressures, pulmonary capillary wedge pressure, and arterial blood pressure, along with the reported heart rate. We collected data on flow based on cardiac output and cardiac index, both as measured by thermodilution and as calculated by the Fick equation (using assumed VO<sub>2</sub>). We also calculated the pulmonary artery pulsatility index ((pulmonary artery systolic pressure-pulmonary artery diastolic pressure)/right atrial pressure), and the right ventricular systolic work index ((pulmonary artery mean pressure—right atrial pressure) × (cardiac index/heart rate)). Finally, we collected data on oxygen extraction, as measured by mixed venous oxygen saturation.

We collected data from the most recent transthoracic echocardiogram, including left ventricular end-diastolic diameter and visually estimated left ventricular ejection fraction. We also collected data from recent cardiopulmonary exercise testing, including peak oxygen consumption (peak VO<sub>2</sub>,), respiratory quotient, ventilatory equivalent of carbon dioxide slope coefficient, and oxygen consumption at anaerobic threshold. The Seattle HF model (SHFM) 1-year projected survival was calculated based on the model developed by Levy et al<sup>16</sup> and available online (https://depts.washington.edu/shfm/); this model uses objective clinical variables and HF treatments to generate estimated projected survival.

We assessed cognitive function in-person using the Montreal Cognitive Assessment (MoCA). The MoCA is a cognitive screening tool, designed for first-line clinicians with an adjusted algorithm for persons with chronic cardiovascular disease (score <24/30) that is 100% sensitive to detect amnestic mild cognitive dysfunction in this population. A MoCA score of 24 was used as the cut point for mild cognitive dysfunction in this study.

Based on the "frailty phenotype," a well-validated measure in older adults, we measured 5 physical frailty criteria: shrinking, weakness, physical exhaustion, slowness, and low physical activity (Figure 2). We measured shrinking

by a self-report of unintentional weight loss of >10 pounds over the last year. We measured weakness of the upper extremities using a hand-held Smedley III Digital Grip Strength Tester (Takei Scientific Instruments, Niigata, Japan). Participants were asked to perform standing maximal isometric contraction with their dominant hand 3 consecutive times with a 5-second rest period between each contraction. Weakness was determined using gender and body mass index cut points based on the frailty phenotype.<sup>3</sup> We also measured weakness of the lower extremities using 5-repeat chair stands. Participants were assessed and timed on their ability to rise out of a chair 5 times without using their arms; a cut point of >12 seconds or inability to rise 5 times indicated weakness.<sup>19</sup> We measured slowness by clocking the time (in seconds) it took a participant to walk 4 m. Participants were asked to walk at their usual speed, starting at 1 m before the start line and walking to 1 m past the finish line. They were permitted to use walking aides (e.g., canes or walkers). Based on a review of cut points for slow gait speed,  $^{20,21}$  we used a cut point of <0.9 m per second to indicate slowness. We measured physical exhaustion using the 13-item Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F; v.4).<sup>2</sup> The FACIT-F captures self-reported tiredness, weakness, and inability to perform activities of daily living as a result of fatigue. The 13 items are rated from 0 (not at all) to 4 (very much); cumulative scores range from 0 to 52 with lower scores indicating more fatigue. Cronbach's \alpha of the FACIT-F in this sample was 0.92. Based on the application of the FACIT-F in the general population, <sup>23</sup> we used a cut point of <17 to identify those with severe physical exhaustion. We measured level of physical activity with the question "During the past week, how much total time did you spend exercising?" Those who reported <1 hour per week (to approximate expending ~300 kcal/week in physical activity) were classified as having low physical activity. We compared responses to this question with the 12-item Duke Activity Status Index, an instrument of functional capacity that assesses activities related to major aspects of physical function<sup>24</sup> and has demonstrated good reliability and validity in HF.<sup>25</sup> Cronbach's  $\alpha$  of the Duke Activity Status Index in this sample was 0.83.

After completing the measures for each of the 5 criteria, the scores were totaled (range 0 to 5; Figure 2). Each participant was then classified as either "non-frail" (0/5 criteria met), "pre-frail" (1-2 criteria met), or "physically frail" ( $\geq$ 3 criteria met). Because of the small numbers in the non-frail group (n = 1), we combined this group with the pre-frail group (n = 24) (i.e., "not physically frail") compared with the "physically frail" group.

Characteristics of the sample are presented using standard descriptive statistics, including measures of central tendency and dispersion. Comparative statistics (Student's *t*, Mann-Whitney *U*, Fisher's exact, or the Pearson's chisquare test) were used to determine significant differences in demographic and clinical characteristics, invasive hemodynamics, and individual physical frailty criteria measures between the 2 groups. Reported effect sizes for individual physical frailty criteria were calculated using, or converted to, Cohen's *d*. Multivariate linear regression was used to compare invasive hemodynamics between groups,

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