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Response to Letter Regarding Article “Characterizing Sex Differences in Physical Frailty Phenotypes in Heart Failure”

Quin E. Denfeld, PhD, RN, FAHA^{a,b}, Kerri Winters-Stone, PhD, FACSM^{a,c}, S. Albert Camacho, MD^b, Christopher S. Lee, PhD, RN, FAAN, FAHA, FHFSA^d

^aOregon Health & Science University School of Nursing, Portland, OR, USA

^bOregon Health & Science University Knight Cardiovascular Institute, Portland, OR, USA

^cOregon Health & Science University Knight Cancer Institute, Portland, OR, USA

^dBoston College William F. Connell School of Nursing, Chestnut Hill, MA, USA

RE: Reply to Martin et al.

Dear Editor,

We thank Martin et al. for their interest in our recent publication on characterizing sex differences in physical frailty in heart failure (HF).¹ We appreciate their insight and suggestions, and we are glad to respond to the key points raised in their letter and continue the dialogue on this important topic.

We measured physical frailty to focus on the physiological aspects underlying frailty in HF (e.g. accelerated aging) in contrast to the multidimensional aspects of frailty often assessed in the clinical context. Both approaches have revealed sex/gender differences in frailty rates² and identified poor clinical outcomes in relation to frailty among adults with HF.³ As Martin et al. point out, however, there may be no sex difference in the relationship between frailty and clinical outcomes. Despite showing that more women than men were considered high frailty using the Clinical Frailty Scale, Kanenawa et al. found that there was no significant interaction for sex when examining the relationship between frailty and two-year all-cause death and HF rehospitalization.⁴ In fact, this finding appears to parallel the geriatric literature, which shows that even though more women are frail, this disparity does not always translate to adverse clinical outcomes. Future research should focus on if frailty in HF is associated with poor clinical outcomes equally in women and men. Moreover, given that physical and multidimensional frailty measures are measuring slightly different constructs, it will be important to distinguish any sex/gender differences between the two approaches.

Corresponding Author: Quin E. Denfeld, PhD, RN, FAHA, Oregon Health & Science University School of Nursing, Mail code: SN-ORD, 3455 S.W. U.S. Veterans Hospital Road, Portland, OR, USA 97239-2941, Phone: +1 (503) 494-7948, denfeldq@ohsu.edu.

Disclosures

The authors reported no direct conflicts related to this letter.

We acknowledge that our sample lacked racial and ethnic diversity, which was a limitation of the race/ethnicity representation in our geographic region. Understanding racial and ethnic disparities in relation to frailty, both physical and multidimensional, is a much-needed area of future research in HF, and we are currently expanding the reach of our research to improve representation of underserved minorities. The weathering hypothesis describes the physiological wear and tear, acceleration of aging, and earlier onset of illness, disability, and death among groups that are chronically exposed to social and economic adversity.⁵ Future research in HF should examine frailty rates by racial/ethnic groups in light of the structural barriers, material hardships, and stereotypes that comprise the experiences of Hispanics, Blacks, and other underrepresented groups.

We considered comparing physically frail men with physically frail women, but the main difficulty with this approach was that women and men are inherently different in several physiological metrics, including echocardiographic and body composition parameters. Thus, any differences between physically frail men with physically frail women could be attributable to normal physiological sex differences. To get around this, we performed an interaction analysis to see if relationships between a particular variable and frailty were different by sex.

Certainly, there is much more to learn in the area of frailty in HF, specifically related to sex differences in outcomes and racial/ethnic differences. We agree that additional psychosocial and contextual characteristics, especially caregiving and self-care, should be factored into future research. These characteristics might elucidate, and ultimately improve, the frailty phenotype among women with HF.

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