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Frailty as a Clinically Relevant Measure of Human Aging

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Frailty, commonly defined as a state of increased vulnerability to potential stressors with decreased physiological reserve owing to aging, has long been considered a geriatric syndrome.[1-3] Research interest in frailty has increased following observations of vast inter-individual heterogeneities in accumulating deficits or functional impairments among functional or biological parameters with the progression of chronological aging.[2] In the last three decades, researchers have attempted to capture frailty in various ways, from operational definitions to counting percentages of deficits arising owing to human aging.[4-6] Although their methods of determining or quantifying frailty differ, studies have shown correlations between frailty spectrums defined by phenotype definition or deficit accumulation.[7]

The clinical relevance of frailty as an aging phenotype has been validated with respect to multiple aspects. By incorporating age-related parameters that are also interconnected to form complex systems of human physiology,[8] the burden of frailty in individuals reflects a systemic disturbance in response to various stressors.[9] Population-based longitudinal studies have assessed the ability of the frailty index in predicting mortality, an unequivocal outcome indicator of human aging.[10,11] Similarly, studies on patients with medical or surgical conditions have reported the superiority of the frailty spectrum in predicting adverse health outcomes compared with conventional measures.[12-14] As a dynamic aging marker that responds to structured interventions, frailty is gradually becoming a cornerstone of geriatric medicine to deliver patient-centered management.[15,16]

With recent advances in clinical and biological knowledge on frailty, the *Annals of Geriatric Medicine and Research* planned a special issue covering this geriatric syndrome from multifaceted aspects of biology, clinical medicine, and public health. In this issue, Ji et al.[17] discussed frailty starting from molecular biology and demonstrated the validity of the frailty index as a measure of human aging compared to omics-based epigenetic clocks and biomarkers. Kwak[18] discussed delirium, a geriatric giant and an important inpatient adverse outcome that occurs disproportionately in frail older people and can often be prevented by appropriate measures. Baek et al.[19] reviewed the establishment and evolution of the Aging Study of Pyeongchang Rural Area (ASPRA), a cohort that was originally designed to determine the natural course of frailty in a Korean rural population and design effective interventional strategies that are feasible even in underserved regions in terms of healthcare resources.

The results of the studies support frailty as a clinically relevant measure of the human aging phenotype, with frailty a plastic and manageable geriatric syndrome. Unknowns still exist regarding the biology of frailty, which require further elucidation. While clinical interventions can improve frailty phenotypes and functional states, it remains unknown whether these improvements lead to the alleviation of the hallmarks of aging. Preclinical and early clinical studies have shown the potential to reverse or attenuate aging phenotypes with modalities related to energy metabolism or cellular senescence.[20-22] These efforts have attracted research interest in rejuvenation and reverse-aging technologies. Moreover, the results of these studies revealed that some parameters of physical frailty improve with the underlying biological aging status.[20] Geriatric interventions with proven clinical efficacies should be assessed with endpoints such as aging biomarkers to provide bi-directional evidence of the relationship between aging biology and frailty to eventually support the biological roles of geriatric interventions in the human aging spectrum.

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CONFLICT OF INTEREST

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