Physiopathology of frailty in older adults: development of biomarkers for its early identification

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The ageing process, characterised by a progressive accumulation of a varied range of molecular and cellular alterations, is widely heterogeneous, and may lead to a large discrepancy between “chronological age” and “biological age”. In the pathway from robustness to disability and dependence related to ageing, frailty is an intermediate stage that has emerged as a more accurate measure of biological age. Frailty is a geriatric clinical syndrome encompassing multisystem age-associated physiological decline, reduced homeostatic reserves, and increased vulnerability to stressors, which increases the risk of negative health consequences such as falls, hospitalization, disability, dependency, and death. Although the pathophysiological mechanisms underlying frailty are not fully understood yet, it is known that frailty can be delayed, or even reversed, if detected in its early stages. Therefore, the development of biomarkers that allow the early detection of this syndrome, before the onset of its clinical manifestations, is crucial for implementing preventive actions and specialized geriatric care that improve the health and quality of life of older adults, as well as reduce associated social and healthcare costs. In this study, a set of parameters related to the ageing process or to age-related diseases were investigated in a population of older adults classified according to their frailty status, to determine their potential validity as biomarkers of frailty. The results obtained support the involvement of genomic instability, hypothalamic-pituitary-adrenal axis dysregulation, Th1-type immune activation and inflammageing in the pathophysiology of frailty, as important driving forces of this geriatric syndrome. Furthermore, certain parameters related to these processes have emerged as promising biomarkers of frailty and may be useful for its early identification.

Funding: This work was supported by the Spanish Ministry of Science and Innovation: MCIN/AEI/https://doi.org/10.13039/501100011033 [Grant PID2020-113788RB-I00], and Xunta de Galicia (ED431B 2022/16).