

Hidden Threat During Quarantine and Transition Phase in Elderly: The Need for Special Precautions

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A global pandemic, COVID-19, has struck 216 countries with more than 9 million cases and 420.000 deaths. In Indonesia alone, 49.000 people have been infected with more than 2.000 deaths.¹ To reduce the transmission rate and break the chain of transmission, various countries in the world require people to limit and mitigate activities outside the house, especially for high-risk groups: the elderly and groups with comorbidities. Although there is no age group protected from SARS-CoV-2 infection, the elderly group shows significantly higher mortality and severity of the disease when compared with young and middle age.² Case fatality rate in the elderly ranges between 8% in patients aged \geq 80 years, 8% in patients aged 70-79 years, and up to 49% in critical cases.³ Other studies also show that the average age of patients who need the intensive care unit (ICU) is older than patients who do not require ICU.⁴

In older age, a higher SARS-CoV-2 viral load is found in the nasopharynx.⁵ This may be explained by the weakened immune system due to aging that increase the likelihood of a cytokine storm⁶ accompanied with the increase in lung ACE2 expression (by ~1.2

times every 10-year increase in age).⁷ The IFN-I, an antimicrobial polypeptide that can attack the SARS-CoV-2 virus, is delayed by the immunosenescence of the host, as well as by the virus itself.⁸ However, a case series mentioned that five older people in China aged 98 to 103 years old could recover from COVID-19 infection.⁹ These findings show that even though the elderly have a higher risk, COVID-19 in elders is not a death sentence. There are other contributing factors besides age that affect prognosis of COVID-19 in elders.

Sarcopenia and frailty were predictors of mortality and morbidity in COVID-19^{10,11} and non-COVID^{12,13} patients. Sarcopenia is a condition characterized by progressive loss of mass and skeletal muscle function, which prevalence increases with age (primary sarcopenia). Sarcopenia can be considered a precursor or primary driver of frailty.¹⁴ Frailty has a broader scope, referred to as "a medical syndrome with multiple causes characterized by diminished strength, endurance, and reduced physiologic functions that increase an individual's vulnerability for developing increased dependency and/or death".¹⁵

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Skeletal muscle tissue comprises approximately 40% of total body weight and 50–75% of all body proteins. Besides playing a mechanical role (to move, supporting the body), skeletal muscle as an endocrine organ can secrete various myokines that can control metabolism. It regulates basal energy, temperature, oxygen consumption, blood glucose level, and body storage of carbohydrates and amino acids.¹⁶ Thus, it is logical that muscle mass reduction impairs the body's response to stress and chronic illnesses.

Although primary aging contributes to muscle mass; nutrient intake, hormonal balance, physical activity, and the presence of trauma/injury has also been shown to influence the rate of muscle mass loss.¹⁷ Kehler et al.¹⁸ showed that not all elderly suffer frailty, some are strong and healthy, and surprisingly frailty can also be found in young people.

Quarantine, transition, or "new normal" periods would likely increase sarcopenia and frailty risk by several aspects. First, psychologically, the elderly are more susceptible to emotional changes, and epidemiological studies show high levels of depression and anxiety (37.1%) during COVID-19.19 Induced by stress, the release of pro-inflammatory cytokines and cortisol trigger catabolism state.¹⁷ Second, the limitation of activity in quarantine will increase the sedentary time. Study shows that reduction in short-term physical activity (14 days) from 10.000 to 1.500 steps/day can significantly affect lower limb lean mass and increase visceral fat, with highlights also impairs insulin sensitivity and dyslipidemia.20 Insulin resistance impairs muscle synthesis as insulin is an anabolic hormone involved in the primary protein synthesis pathway, the mammalian target of rapamycin (mTOR) pathway, through the insulin / PI3K / Akt signaling.¹⁷ In addition to body composition, step reduction also increases pro-inflammatory cyto-kines: TNF- α and C-reactive protein, by approximately 12% and 25% respectively, and reduced myofibrillar protein synthesis by approximately 26%, which would enhance protein degradation.21

Third, physiologically, anabolic resistance and cellular dysfunction occur due to the build-up of reactive oxygen species in the elderly. Anabolic resistance decreases the sensitivity of protein synthesis to anabolic stimuli such as nutrition and exercise. In other words, it takes an enormous amount of amino acids and exercises stimulation to induce protein synthesis. The rate of muscle protein synthesis that cannot keep up with the rate of protein degradation will result in loss of muscle mass and strength.¹⁷ Muscle loss is approximately 8% per decade from 40 to 70 years, and increases to 15% per decade after this.²² Moreover, nutrient intake in elderly is usually inadequate due to decreased appetite, decreased sensory function, tooth disorders, and cognitive impairment.¹⁴ From the social aspect, most of the elderly experience a decrease in their ability to prepare food, cognitively or physically, so that elderly who live without families and not in a nursing home, will have difficulty accessing restaurants during this time.²³

Fourth, the limitation of outdoor activities and lack of exercise in the elderly results in a lack of sun exposure. Despite being in a tropical country, 35% of the elderly living in institutionalized care units in Indonesia is having Vitamin D deficiency.24 In addition to its role in the immune and antimicrobial system (cathelicidin and defensin), Vitamin D also exerts molecular effects through Vitamin D receptors (VDR) within the muscle cell. People with 25(OH)D level <25 nmol/l have an odds ratio of 2,57 (based on handheld strength) and 2,14 (based on muscle mass) higher risk for experiencing sarcopenia if compared to people with levels of 25(OH) $D > 50 \text{ nmol/l.}^{25}$ Lastly, the pressures of other health problems or comorbidities also influence the metabolism that leads to the catabolic state or induces anorexia.¹⁷

Hence, additional health measures should be done as precautions to slow the progression of frailty in elderly. Boreskie et al.²⁶ summarized some of the efforts that can be made as "SAVE" (Socialization, Adequate nutrition, Vitamin D, and Exercise). To regain social relations, the application of telecommunication can be the answer. The general guidelines of 150 minutes of moderate to vigorous physical activity per week to promote health and functional capacity might seem hard to achieve in the elderly in the current situations.²⁷ Therefore, specific guidance may be needed for the elderly. Passive movements assisted by caregivers can also be performed for the elderly with limited mobility.²⁸ Studies show reallocation of sedentary behavior for 15 minutes per day and one hour per day to moderate-intensity activities can reduce the risk of sarcopenia by 15% and 50%, respectively.²⁹

To make an appropriate meal plan based on individual needs, we suggest that Vitamin D level and nutritional intake (using food record) should promptly be assessed.

Adequate protein intake in the elderly to maintain and regain muscle is 1,0-1,2 g/kg body weight, or 1,2-1,5 g/kg body weight in the elderly with acute or chronic disease.¹⁴ In addition to the amount of intake, protein distribution also play an essential role in muscle synthesis. A balanced distribution of protein intake promotes optimal protein synthesis.¹⁷ Vitamin D can be obtained through a combination of oral intake and sunlight exposure, with the target of 50 nmol/l 25(OH)D. This Institute of Medicine recommendation is based on the limit that covers at least 97,5% of the population.³⁰ Evaluating and monitoring body mass index alone is not enough for the elderly because muscle loss is also accompanied by an increase in fat mass, called 'sarcopenic obesity'.³¹ We advise using a validated measurement, such as dual-energy X-ray absorptiometry (DXA) or the more affordable bioelectrical impedance analysis (BIA), to assess elderly body composition timely.

In conclusion, precautions must be taken holistically. All of these efforts will not succeed without the control of existing comorbidities. Therefore, to make these precautions practical, education is needed for all medical staff, community, and especially caregivers, not only to avoid COVID-19 infection, but also synergistically maintain the health of the elderly optimally during the quarantine and transition phase.

Conflict of Interest Statement

This editorial was written in the absence of any financial or commercial relationships.

Funding

No financial assistance or sponsor support this editorial.

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