Review of: "[Review] Sarcopenia in Coronavirus Disease (COVID-19): All to Know from Basic to Nutritional Interventions from Hospital to Home"

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Potential competing interests: No potential competing interests to declare.

The review is very interesting and is unique in its kind.

Paragraph “Importance and the triangle link of Sarcopenia, COVID-19 and outcome”: I suggest considering the following points.

The triangle link between Sarcopenia, COVID-19, and outcomes refers to the interconnected relationship between these three factors and their impact on health outcomes in individuals. Sarcopenia can exacerbate the negative effects of COVID-19 and impact health outcomes in several ways:

- Disease severity: sarcopenia is associated with weakened immune function and increased susceptibility to infections, including respiratory infections like COVID-19. Individuals with Sarcopenia may have a higher risk of developing severe forms of COVID-19, requiring hospitalization, and experiencing longer recovery periods.

- Respiratory function: sarcopenia affects the respiratory muscles, reducing lung capacity and respiratory function. In the context of COVID-19, this can lead to further respiratory complications and increase the risk of respiratory failure in individuals with Sarcopenia.

- Functional decline: COVID-19 can result in prolonged hospitalization and bed rest, which can accelerate muscle loss and functional decline in individuals with Sarcopenia. This may lead to increased disability, decreased mobility, and difficulties in performing activities of daily living.

- Mortality: sarcopenia is associated with an increased risk of mortality in various populations. When combined with COVID-19, the presence of Sarcopenia can contribute to higher mortality rates. The weakened immune response, respiratory complications, and functional decline associated with Sarcopenia can make individuals more vulnerable to severe COVID-19 outcomes.

Understanding the triangle link between Sarcopenia, COVID-19, and outcomes is important for healthcare providers and policymakers. It highlights the need for targeted interventions to prevent and manage Sarcopenia, especially in older adults and high-risk populations. Such interventions can include physical exercise, proper nutrition, and other strategies aimed at preserving muscle mass, strength, and function.

By addressing Sarcopenia, healthcare professionals can potentially improve the prognosis and outcomes of individuals

affected by COVID-19.

Paragraphs “The mechanism between COVID-19 and Sarcopenia” and “HealthCare During Hospitalization”: I suggest restructuring the paragraphs according to the mechanisms underlying the link between COVID-19 and Sarcopenia.

- Impaired immune response: One of the key mechanisms linking COVID-19 and Sarcopenia is the impaired immune response observed in both conditions. Sarcopenia is associated with chronic low-grade inflammation. This systemic inflammation negatively affects the immune system's ability to mount an effective response against viral infections, including COVID-19. Consequently, individuals with Sarcopenia may be more susceptible to severe COVID-19 outcomes.

- Cytokine storm and muscle wasting: COVID-19 infection can trigger an exaggerated immune response known as a cytokine storm. The excessive release of pro-inflammatory cytokines, such as interleukin-6 (IL-6), can contribute to muscle wasting and accelerate the progression of Sarcopenia. Elevated levels of IL-6 and other inflammatory markers observed in COVID-19 patients have been associated with increased muscle protein breakdown, impaired muscle regeneration, and decreased muscle strength.

- Physical inactivity and bed rest: COVID-19 often necessitates hospitalization, bed rest, and prolonged periods of inactivity. This enforced immobilization can exacerbate the muscle loss characteristic of Sarcopenia. Bed rest leads to rapid muscle atrophy, weakness, and functional decline, contributing to a vicious cycle of Sarcopenia progression. Furthermore, reduced physical activity and prolonged immobilization during the recovery phase of COVID-19 can further exacerbate Sarcopenia, impairing functional recovery and increasing the risk of long-term disability.

-Respiratory muscle dysfunction: Respiratory muscle weakness is a common feature of both COVID-19 and Sarcopenia. In COVID-19 patients, respiratory muscle dysfunction can lead to respiratory distress, the need for mechanical ventilation, and prolonged weaning from ventilatory support. The combination of pre-existing respiratory muscle weakness due to Sarcopenia and the additional strain imposed by COVID-19 infection can result in more severe respiratory complications and poorer outcomes.

..with focus on Endocrinology:

- Impact of inflammation: Inflammation plays a central role in both COVID-19 and Sarcopenia. The cytokine storm observed in severe COVID-19 cases leads to the release of pro-inflammatory cytokines, including interleukin-6 (IL-6). Elevated IL-6 levels contribute to muscle protein breakdown and impair muscle regeneration. Furthermore, chronic low-grade inflammation associated with Sarcopenia disrupts the endocrine system, leading to alterations in hormone levels that affect muscle homeostasis.

- Hormonal imbalance: Endocrine dysregulation is a prominent feature in both COVID-19 and Sarcopenia. COVID-19 infection can disrupt the hypothalamic-pituitary-adrenal (HPA) axis, resulting in adrenal insufficiency and decreased cortisol production. Cortisol is an important hormone involved in muscle protein metabolism and immune function. The

reduced cortisol levels in COVID-19 patients may exacerbate muscle wasting and hinder the body's ability to combat the viral infection.

Additionally, Sarcopenia is associated with alterations in anabolic hormones such as growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Reduced GH secretion and impaired IGF-1 signaling contribute to muscle loss and impaired muscle regeneration observed in Sarcopenia. COVID-19 may further disrupt this delicate hormonal balance, exacerbating muscle wasting and compromising the body's ability to recover from muscle damage.

- Vitamin D deficiency: Vitamin D deficiency has been implicated in the pathogenesis of both COVID-19 and Sarcopenia. Vitamin D plays a crucial role in immune function, muscle health, and endocrine regulation. Low vitamin D levels have been associated with increased susceptibility to respiratory infections, including COVID-19, and are also prevalent in individuals with Sarcopenia. Vitamin D deficiency can further aggravate muscle wasting and impair immune response, leading to a vicious cycle of detrimental effects on both conditions.

- Sedentary lifestyle and insulin resistance: Prolonged bed rest and physical inactivity during COVID-19 infection can contribute to muscle loss and insulin resistance. Insulin resistance is a hallmark of Sarcopenia and is associated with impaired muscle protein synthesis and increased muscle protein breakdown. COVID-19-induced immobility exacerbates this insulin resistance, leading to further muscle wasting and metabolic dysfunction.

A revision of the wording and English is needed.