Acute Sarcopenia in Elderly with COVID-19: An Overlooked Problem

I Gusti Putu Suka Aryana1*, Dian Daniella2, Raden Ayu Tuty Kuswardhani1, Siti Setiati3

INTRODUCTION

Morbidity and mortality rates of coronavirus disease-19 (COVID-19) are particularly high in older people. In Indonesia, older people contributed to 38.6% of COVID-related deaths. Less than 65 years old population in European countries and Canada has 30 to 100-fold lower risk of COVID-19 related deaths than those > 65 years old, 16- to 52-fold lower risk in the United States of America (USA) locations and less than 10-fold in the the India and Mexico. One of the less known morbidities and mortality risk factors in the elderly with COVID-19 was sarcopenia. The European Working Group on Sarcopenia in Older People (EWGSOP), International Working Group on Sarcopenia (IWGS), and Asian Working Group for Sarcopenia (AWGS) all define sarcopenia as loss of skeletal muscle mass and muscle function; either low muscle strength or low physical performance. Prevalence of sarcopenia in the elderly ranges between 3% to 59%, with the highest prevalence in individuals aged 80 years or above. Acute sarcopenia is an incident of sarcopenia within six months, normally following a stressor event.

The risk of acute sarcopenia is higher in older patients with COVID-19 than in younger patients. In the short term, sarcopenia was associated with increased risk of mortality, ICU admission, and mechanical ventilation in COVID-19 patients. Elderly with sarcopenia have a higher risk of cardiovascular disease, diabetes mellitus, osteoporosis, and lower quality of life in the long term. In return, the study stated that long-term bed rest due to a critically ill state and mechanical ventilation that usually occurs in the elderly with COVID-19 would further aggravate acute sarcopenia. Factors contributing to acute sarcopenia are multiple, as immune response also plays a role. It is important to identify contributing factors to acute sarcopenia as it can help clinicians prevent and manage it in the elderly better.

Studies regarding factors contributing to acute sarcopenia in the elderly with COVID-19 are limited and in clinical practice, sarcopenia is often not assessed and did not contribute to management decision-making. This paper aims to identify contributing factors of acute sarcopenia in the elderly with COVID-19 and their effect on treatment outcomes.

COVID-19 in Elderly

COVID-19 in the elderly is usually presenting with atypical symptoms and high mortality. Gan et al. did a retrospective analysis of 122 older patients (mean age 81 ± 8 years old). The most common presenting complaints were falls in 18 patients (36%), reduced mobility or generalized weakness in 18 (36%), and delirium in 11 (22%). Reduced mobility or generalized weakness as presenting complaints showed that acute sarcopenia might exist on pre-admission. A meta-analysis of 13,624 elderly stated that there are a high proportion of patients with severe disease (51%), critical illness (22%), and high mortality (11%). Eighty-four percent of patients required oxygen support and 21% required mechanical ventilation.

One of contributing factors to morbidity and mortality in the elderly with COVID-19 is acute sarcopenia. SARS-CoV-2 infection was causing acute sarcopenia. There are multiple contributing factors to acute sarcopenia in COVID-19, such as inflammation, malnutrition, bedrest and physical activity, COVID-19 treatment, and depression (Figure 1).

ABSTRACT

The coronavirus Disease-19 (COVID-19) pandemic was announced in March 2020 by World Health Organization (WHO). Studies showed that the elderly had higher morbidity and mortality rates. Acute sarcopenia in the elderly with COVID-19 is an overlooked problem. Inflammation, malnutrition, immobilization, a side effect of COVID-19 treatment, depression, and hormonal dysregulation contributed to acute sarcopenia in COVID-19, especially in the elderly. Muscle quantity can be assessed with different techniques such as imaging or anthropometric measurements in diagnosing sarcopenia. Imaging such as CT scan was widely used in multiple studies. Still, anthropometric measurements are more fit in developing countries because they are widely available, safe, do not require special skills, and fit in low-resources facilities. Muscle strength can be assessed with grip strength. Acute sarcopenia was associated with immune dysregulation and cytokine storm, length of stay and readmission, and ICU admission and mechanical ventilation. These will contribute to high mortality in sarcopenic elderly with COVID-19.

Keywords: Sarcopenia, Muscle Loss, Muscle mass, Elderly, Covid-19.


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Compared to young people, the elderly have higher systemic basal inflammatory mediators. This phenomenon happens independently of immune challenges and is known as inflammaging. Inflammaging is a risk factor of chronic diseases associated with aging and immunosenescence. Immunosenescence is an overall change to the immune system as we age. Aged dendritic cells have a reduced ability to produce type I interferon (IFN), ultimately reducing the expression of antiviral IFN-stimulated genes (ISGs) and enhancing viral replication. Viral replication leads to cell death and damage, resulting in a hyperinflammatory state.21

Acute Sarcopenia in COVID-19
European Working Group on Sarcopenia in Older People 2 Guideline 2018 defined probable sarcopenia as low muscle strength, confirmed sarcopenia as low muscle strength, low muscle quantity or quality, and severe sarcopenia as low muscle strength, low muscle quantity or quality, and low physical performance. Acute sarcopenia is defined as sarcopenia that happens within six months.4 Different techniques can be used to assess skeletal muscle quantity or quality in COVID-19 patients. Multiple studies showed that CT scan, Magnetic Resonance Imaging (MRI), Dual-energy X-ray absorptiometry (DXA), Ultrasound (USG), Bioelectrical Impedance Analysis (BIA), electromyography, and the anthropometric measures could be used for this purpose.4 Computed tomography modality is widely used due to its dual function. It can be used to assess the pulmonary extension of the disease while assessing acute sarcopenia. The muscle used to assess sarcopenia was paravertebral muscle in T524 and T1223 and psoas muscle in L3.9 There are no cutoff values for diagnosing sarcopenia as multiple studies used parameters, such as muscle mass defined as Hounsfield unit (Hu) values <30,10 lower quartile skeletal muscle index25, and total muscle area.9 Derstine et al. measure muscle at each vertebral level between T10 to L5. They suggested using L3 as the primary site for CT sarcopenia measurements. In conditions where L3 is not available, alternative levels in order of preference are L2, L4, L5, T12, T11, and T10.24 As CT has a high radiation risk and a high chance of spreading infection in mobilization to the radiology room, USG could be an alternative. Ultrasound can be done bedside and no radiation. Corradi et al. used USG on diaphragm to assess the risk of mechanical ventilation and mortality.11 In developing countries, assessing muscle quantity with radiology modalities are scarce due to limited resources.4 Anthropometric measurements are low-cost alternative. They consist of mid-upper arm circumference, calf circumference and skin fold thickness. Calf circumference < 31 cm has been associated with disability. Anthropometric measurements are widely available, safe techniques, do not require special skills and fit in low-resources facilities, but they are prone to error especially in edema and obese patients.4

Muscle strength can be assessed with grip strength and chair stand test.5 One hundred fifty COVID-19 patients were assessed for grip strength. Lower grip strength was found in female patients and high CRP, ferritin, and LDH.25 Low grip strength is associated with higher all-cause mortality, cardiovascular morbidity, and mortality and mechanically ventilation re-intubation rate. It is strongly correlated with respiratory muscle strength and lung capacity. The advantages of hand-grip strength are non-invasive, simple, and inexpensive.28 Physical performance can be assessed with gait speed and a timed-up-and-go test. Usually, physical performance cannot be assessed due to the weak state of COVID-19 patients.5

Sarcopenia increased the risk of mortality in critically ill patients compared to those without sarcopenia (OR = 2.28).7 Low-muscle area was associated with higher mortality compared with normal-muscle area in females (47.5% versus 20%; p=0.008) and in males (32.3% versus 7.5%). The odds ratio for the low-muscle area was 4.3.3 Acute sarcopenia has a negative effect on the elderly with COVID-19, such as a higher risk of ICU admission10 and mechanical ventilation11 higher length of stay23, and hospital readmission15, and immune senescence.28 All of this contributed to a higher risk of mortality.7

Contributing Factors to Acute Sarcopenia in Elderly with COVID-19

Inflammation
The Elderly has dysregulated immune response resulting in atypical presentation and severe COVID-19.29 Higher degree of inflammation leads to more severe COVID-19. A cohort of 163 COVID-19 patients showed that biomarkers such as Interleukin (IL)-6, lactate dehydrogenase (LDH) and procalcitonin were independently associated with death and mechanical ventilation dialysis need.30 Corticosteroid usage in severe COVID-19 patients reduced mortality and the need for mechanical ventilation.31

Inflammation in COVID-19, especially severe inflammation, contributes to acute sarcopenia.32 Piotrowicz et al. stated that a high degree of inflammation, marked by elevated concentration of C-reactive Protein (CRP), IL-6 and Tumor Necrosis Factor-α (TNF-α), strongly correlated with frailty.32 Reactive oxygen species (ROS) is especially high in aged muscle, especially during inflammation. Both ROS and TNF-α will stimulate the production of a pro-oxidant names myostatin. In the elderly, myostatin will inhibit the growth of skeletal muscle by hindering myoblast proliferation as well as fostering muscle protein degradation (Table 1).33

The high degree of inflammation also leads to multiorgan damage.33 Puthucheary et al. analyzed 63 critically ill patients (mean age of 54.7 years old). On day 10, rectus femoris muscle mass was significantly reduced (~17.7%). The decrease was greater in patients who experienced multiorgan failure (~15.7%) than single organ failure (~3.0%). It might be happened due to decrease protein synthesis and independent of nutritional load with higher protein breakdown.34

Age also contributes to inflammation. In aging, inflammaging that is characterized by chronic low-grade inflammation develops.35 In chronic low-grade inflammation, IL-6 promotes pro-inflammatory properties, ultimately leading to muscle catabolism and skeletal muscle function loss.36

Table 1

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
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<tbody>
<tr>
<td>Rectus femoris muscle mass</td>
<td>Reduced</td>
</tr>
<tr>
<td>Axial skeletal muscle</td>
<td>Reduced</td>
</tr>
<tr>
<td>Respiratory muscle strength</td>
<td>Reduced</td>
</tr>
<tr>
<td>Lung capacity</td>
<td>Reduced</td>
</tr>
<tr>
<td>Immune system</td>
<td>Reduced</td>
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</table>
Malnutrition
A balanced diet and nutritional status contribute to a better outcome in COVID-19 patients. Diet consists of healthy plant foods such as fruit and vegetable associated with a lower risk of COVID-19 and severe COVID-19. 

Inflammation in COVID-19 is associated with a catabolic state and anabolic resistance, leading to increase nutritional demand, particularly protein. Wierdema et al. analyzed 407 hospitalized COVID-19 patients (60% in the Intensive Care Unit (ICU) and 40% in the nursing ward). The mean age was 64.8 ± 12.4 years. At admission, 67% of patients were overweight and during a hospital stay, 21% showed acute weight loss (> 5 kg). Most of these patients (85%) were admitted to the ICU at any point in time and prevalent to sarcopenia. Acute weight loss may contribute to acute sarcopenia.

Nutritional complaints also contributed to acute sarcopenia. More than 90% of COVID-19 patients experience some form of nutritional complaints during hospitalization, especially loss of smell and taste. Aging also contributed to anorexia. This phenomenon is called anorexia of aging and is associated with a reduction in dietary diversity and oral intake, increased risk of malnutrition, sarcopenia, and frailty. Sarcopenia also affects masticatory muscle and suprahypoid muscles. It is associated with decreased masticatory and swallowing function, which will further exacerbate malnutrition.

Low glycemic index food is important to prevent anabolic resistance, leading to age-related glycemic dysregulation. The fiber in such food further enhances healthy gut microbial fermentation. This results in the production of acetate, propionate, and butyrate that support protein delivery to skeletal muscle. Other foods suggested in slowing sarcopenia are creatine-rich foods (e.g., fish and meat), glutamic acid-rich foods (e.g., soy and egg), tryptophan-rich foods (e.g., milk and peanuts), long-chain polysaturated fatty acids and antioxidant supplements (e.g., selenium, vitamin A, vitamin C, vitamin E, and β-carotene).

An unhealthy diet also contributes to sarcopenia. COVID-19 patients usually have unhealthy diets as they tend to be inactive with lower food intake. The gut microbiome is altered in inactivity, poor dentition, altered food intake, and low fiber diet, resulting in local mucosal inflammation.

Malnutrition and obesity also predispose certain risks to sarcopenia, hence the term sarcopenic obesity. Sarcopenic obesity is a recognized condition defined by reduced muscle mass with increased fat mass. Higher body mass index (BMI) is associated with reduced gait speed and a lower degree of physical function, therefore contributing to sarcopenia. Wilkinson et al. stated that sarcopenic obesity in elderly COVID-19 patients (mean age 70 years old) was related to more severe COVID-19 (odds ratio (OR) 2.619). Obesity affects heightened inflammatory response in acute illness, therefore leading to severe forms of COVID-19 and acute sarcopenia.

Vitamin D deficiency is common in COVID-19 patients as some guidelines suggested using vitamin D as one of the treatments for COVID-19. Kostoglou-Athanassiou et al. studied 50 acutely ill patients and 50 healthy control subjects. It was stated that 25(OH)D3 levels were significantly lower in the acutely ill patients compared with the control group (11.74 ± 0.88 ng/ml vs. 24.66 ± 1.60 ng/ml). The level of 25(OH)D3 is also inversely related to CRP and procalcitonin (PCT) levels. This evidence shows that low 25(OH)D3 levels strongly correlate better to the degree of inflammation rather than as a risk. In COVID-19, especially in the elderly, high-degree inflammation usually occurs. A high degree of inflammation leads to vitamin D deficiency. Previously vitamin D is associated with osteoporosis, but a recent review by Ceglia L stated that vitamin D might be associated with skeletal mass. In its biologically active form, 1,25-dihydroxy vitamin D [1,25(OH)2D] exerts its actions by binding to a vitamin D receptor (VDR). Through this receptor, 1,25(OH)2D promotes the fast activation of Mitogen-Activated Protein Kinase (MAPK) signaling pathways, which initiate myogenesis and cell proliferation. Biopsies of skeletal muscle in adults with vitamin D deficiency have shown predominantly type II muscle fiber atrophy. Low vitamin D has been associated with sarcopenia, falls, hip fractures, and death in the elderly. It shows that deficiency or low vitamin D levels may contribute to acute sarcopenia in the elderly with COVID-19. The elderly with supplemented vitamin D have a lower 3-month mortality rate than those without; therefore, it is suggested to give supplemental vitamin D.

Immobilization
Hospitalized COVID-19 patients have a prolonged period of bed rest and reduced physical activity. Physical training proved beneficial in COVID-19 patients as it improved the symptoms, lowered the duration of mechanical ventilation, and improved the quality of life. Elderly on bedrest was prone to loss of muscle mass. Even in not hospitalized COVID-19 patients, patients who contracted COVID-19 suffered immense fatigue, resulting in reduced physical activity. Ten days of bed rest in healthy elderly cause significant acute changes, such as a decrease in muscle protein synthesis (-30%), whole-body lean mass (−1.50 kg), lower extremity lean mass (−0.95 kg), and strength (−15.6% chance).

The Elderly are more prone to muscle mass and strength loss than younger patients in the immobilized state. Three pathways contributed to skeletal muscle atrophy, such as muscle atrophy F-box (MAFbx) and muscle ring finger 1 (MuRF1) pathway, insulin-like growth factor 1 (IGF1)-AKT-mammalian target of rapamycin (mTOR) pathway, and myostatin pathway. Immobilization will induce MAFbx and MuRF1, leading to proteolysis and decreasing protein synthesis. Downregulation of the IGF1-AKT-mTOR pathway induces proteolysis, myostatin activates Smad3 that will interact in the AKT-mTOR pathway that inhibits protein synthesis.

Physical activity helps maintain the shape and structure of muscle fibers. It will alter skeletal muscle mitochondrial and metabolic activities, contributing to muscle mass loss. Moderate to vigorous exercise helps restore muscle mass and prevents the development of sarcopenia. It restores and corrects altered metabolism within skeletal muscle. This showed that physical inactivity in hospitalized and
non-hospitalized COVID-19 patients contributed to acute sarcopenia.33

COVID-19 treatment

Parenteral corticosteroids have been used in patients with severe COVID-19 disease and respiratory failure.34 Paddon-Jones et al. stated that prolonged inactivity and hypercortisolemia would give persistent catabolic stimulus that exacerbates muscle loss. Patients were given hydrocortisone sodium succinate intravenously (day 1 and 28) and orally (day 2-27) to reproduce plasma cortisol concentrations consistent with trauma or illness (approximately 22 µg/dl). They found an acute 28.4 +/- 4.4% loss of leg extension strength and a 3-fold greater loss of lean leg mass (1.4 +/- 0.1 kg) than bed rest alone.39 Research on the effect of corticosteroid administration on cortisol levels in COVID-19 patients is still needed. Stress and inflammation also contribute to higher cortisol levels, therefore, it is suggested that corticosteroids should be given as needed in COVID-19 patients to prevent unwanted hypercortisolemia. Plus, the effect of muscle loss may be exacerbated in elderly patients as they are usually physically inactive.

Other drugs, such as antibiotics, may increase the risk of sarcopenia or aggravate it. Antibiotics could lead to gastrointestinal symptoms such as nausea, anorexia, and diarrhea. These complications will hinder nutritional adequacy in the elderly with COVID-19.36 Sedative in ICU may promote delirium leading to a higher risk of acute sarcopenia.35 Delirium was associated with sarcopenia and risk of sarcopenia in the elderly.34 Vice versa, Zuchelli et al. stated that low muscle mass is independently associated with delirium (OR: 1.50). Delirium and sarcopenia are both triggers with dysregulated immune responses. Therefore, these two conditions are often associated. Sarcopenic patients are at higher risk of developing delirium even when therapeutic drug dosages are used due to changes in body composition.55

Depression

The COVID-19 pandemic constitutes extraordinary health problems, including mental health problems. The prevalence of depression was 25% from a meta-analysis in 2020. This number is seven times higher than in 2016 (3.44%). It suggests an important impact of the COVID-19 outbreak on people's mental health.57 Wang et al. analyzed 14,877 COVID-19 patients and found that mental disorders such as anxiety and depression are associated with a higher risk of COVID-19 infection and mortality.57 Therefore, clinicians should pay attention to patients with mental disorders as they will have worse outcomes, especially the elderly. Depression was associated with sarcopenia (OR 2.23) and low muscle strength (OR 1.94).58 Study included 836 patients who also stated that depression was associated with sarcopenia and low BMI.59 Sarcopenia and depression were associated due to neurotrophins that promote neuronal survival and differentiation produced by the brain and skeletal muscle and are associated with the mood and muscle regeneration.58 Another inactivity, low-grade inflammation, and oxidative stress contribute to sarcopenia in depressed patients.55 With association to lower physical activity, malnutrition, and inflammation, depression may contribute to acute sarcopenia in the elderly with COVID-19.

Hormonal dysregulation

Sex steroids such as estrogen and testosterone decline with aging, contributing to muscle loss. Testosterone blocks the production of myostatin and ROS, inhibits apoptosis, potentiates myosatellite stem cells, accelerates muscle insulin growth factor-1 (IGF-1) expression, regulates skeletal muscle metabolism, and increases muscle protein synthesis rate and muscle mass in an older adult. Growth hormone (GH) decrease in aging will also lower muscle mass. Another hormonal dysregulation in sarcopenia is insulin resistance. The inflammation blocks IGF-1 and promotes insulin resistance giving rise to anabolic resistance, catabolism, and adipose infiltration in skeletal muscle.53

CONSEQUENCES OF ACUTE SARCOPENIA IN ELDERLY WITH COVID-19

Immune dysregulation and cytokine storm

The relationship between sarcopenia and infection has been shown in multiple studies. Cosqueric et al. analyzed 101 patients and found that sarcopenic elderly have a higher risk of infection (relative risk (RR): 2.1).58 Nakanishi et al. also stated that sarcopenia was associated with non-surgical site infection.26

**Figure 1.** Contributing Factors to Acute Sarcopenia in Elderly with COVID-19.16-18,22,33,39,41,43,59
Table 1. Contributing factors to acute sarcopenia in COVID-19.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Mechanism</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation</td>
<td>COVID-19 inflammation stimulates myostatin production that inhibits skeletal muscle growth.</td>
<td>16,22,33</td>
</tr>
<tr>
<td></td>
<td>Multiorgan damage patients have decreased protein synthesis and higher protein breakdown.</td>
<td>34,16</td>
</tr>
<tr>
<td></td>
<td>Inflammaging promotes a pro-inflammatory state, leading to muscle catabolism and loss of skeletal muscle function.</td>
<td>36,35,60,61</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Due to loss of smell and taste and aging, malnutrition leads to muscle mass loss.</td>
<td>17,38,39</td>
</tr>
<tr>
<td></td>
<td>Obesity reduces gait speed and physical function with an increased inflammatory response</td>
<td>40,41</td>
</tr>
<tr>
<td></td>
<td>Vitamin D deficiency correlated with lower inflammation response and lower skeletal mass</td>
<td>42,43,44</td>
</tr>
<tr>
<td>Immobilization</td>
<td>Immobilization decreases protein synthesis, whole-body lean mass, lower extremity lean mass, and strength.</td>
<td>6,18,33,62</td>
</tr>
<tr>
<td>COVID-19 treatment</td>
<td>Parenteral corticosteroid exacerbated muscle loss.</td>
<td>34,19</td>
</tr>
<tr>
<td></td>
<td>Antibiotics with gastrointestinal symptoms hinder nutritional adequacy.</td>
<td>34,63</td>
</tr>
<tr>
<td>Depression</td>
<td>Same neurotrophins associated with mood and muscle regeneration.</td>
<td>34,54,36,64</td>
</tr>
<tr>
<td></td>
<td>Depression causes inactivity, low-grade inflammation, and oxidative stress</td>
<td>20,67,68</td>
</tr>
<tr>
<td>Hormonal dysregulation</td>
<td>Decreasing sex steroids such as estrogen and testosterone</td>
<td>33,69,70</td>
</tr>
<tr>
<td></td>
<td>GH decrease</td>
<td>33,71,72</td>
</tr>
<tr>
<td></td>
<td>Insulin resistance due to inflammation</td>
<td>33,73,74</td>
</tr>
</tbody>
</table>

**Abbreviations:** GH, growth hormone

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The muscle has been recognized as an organ with immune regulatory properties. Skeletal muscle modulates immune function by signaling through secreting myokines. Myokines such as IL-6, IL-7, and IL-15 have been shown to affect the immune system, with IL-7 and IL-15 being inversely correlated with age, hence the lower immune system in the elderly. IL-15 maintains immune function, stimulating myogenesis and reducing adipose tissue distribution. Reduced IL-15 will lower natural killer (NK)-cells with neutrophil and lymphocyte function. The pro-inflammatory effect of IL-6 includes enhanced T-cell recruitment, antibody production, and lymphocyte trafficking. Therefore, in sarcopenia, insufficient myokine signaling disrupts immune system function. Acute sarcopenia may affect muscle cell signaling needed for immune regulation and maintenance, which will lead to a longer time to recover from COVID-19, a higher risk of secondary infection and, On the other side, the dysregulated immune system also reflects the hyperinflammatory state in sarcopenic elderly that is characterized by higher cytokine. Maladaptive response initially in the elderly to the virus will cause higher

**Figure 2.** Consequences of Acute Sarcopenia in Elderly with COVID-19.9,21,22,27,28,36,44

**Abbreviations:** LOS, length of stay; ICU, intensive care unit.
cytokine release. All of these conditions will cause a cytokine storm. Cytokine will attract many inflammatory cells, such as neutrophils and monocytes, resulting in the infiltration of inflammatory cells to cells, especially lung tissue, causing lung injury. Cytokine storm is associated with a more severe form of COVID-19, mechanical ventilation need and mortality (Figure 2).  

**Length of stay and readmission**

Kim et al. defined sarcopenia as the lowest quartile of skeletal muscle index, which was ≤ 24 cm²/m² for men and ≤ 20 cm²/m² for women. The muscle assessed was the T12 paravertebral muscle. They found that sarcopenia at baseline was associated with mortality (OR 3.8) and longer hospital stay (median 55 vs 28 days).(23) Length of stay was usually higher due to ICU admission and a more severe form of COVID-19.

Yang et al. analyzed 49 elderly sarcopenic patients. They found that during the three-year follow-up period, sarcopenic patients were more likely to be readmitted to the hospital than subjects without sarcopenia (71% vs 56.3%).(27)

**ICU admission and mechanical ventilation**

Sarcopenia was associated with an increased risk of ICU admission(10) and mechanical ventilation.(11) Giraudo et al. stated that muscle loss of T12 paravertebral muscle is a predictor of ICU hospitalization in COVID-19 patients. The study included one hundred fifty patients with a mean age of 61.3 ± 15 years old. Chest CT was done during the first three weeks of hospitalization (average 5.5 ± 4 days) and muscle mass was defined with Hu. Patients in ICU have significantly lower Hu values (29 ± 24 vs. 39.4 ± 12 Hu). A value of 34 Hu showed 71.7% sensitivity and 53% specificity for ICU admission. It stated that muscle loss (Hu values < 30) was associated with more severe disease, as seen in higher Lactate Dehydrogenase (LDH) and CRP.  

Schiaffino et al. did a chest CT scan on admission in COVID-19 patients and found the same result. The muscle assessed was T5 paravertebral muscle. It stated that the lower than median T5 paravertebral muscle area showed higher OR for ICU (OR 4.3).(21)

Corradi et al. retrospectively reviewed records of 77 older COVID-19 patients (mean age 59 (51-77 years). The patient who needed mechanical ventilation or died had thinner diaphragms than those who did not (2.0 vs 2.2 mm). A diaphragm ultrasound was done within 36 hours from admission.(11) After being intubated, Kou et al. found that sarcopenia is an independent risk factor for the difficulty to weanS. Ninety-six intubated patients with a median age of 73 years old were included. Sarcopenia was assessed by calculating Total Psoas Muscle Area (TPA) at L3 with a CT scan upon ICU admission. A TPA less than 385 mm²/m² for women patients or 545 mm²/m² for men patients was defined as sarcopenia.  

**High mortality**

Sarcopenic elderly with COVID-19 has a high mortality. Immune dysregulation causing secondary infection or cytokine storm is one contributing factor to mortality.(21,26,28) After COVID-19 infection, especially in mechanical ventilated patients, the risk of sarcopenia is high. Inspiratory muscle training was proven to improve pulmonary functions, dyspnea, functional performance, and quality of life of weaned mechanical ventilated COVID-19 patients.(46) In COVID-19 management in the elderly, we believe that early detection and interventions of acute sarcopenia are needed. Interventions consist of nutrition and physical training management.(34)

**CONCLUSION**

Inflammation, malnutrition, immobilization, a side effect of COVID-19 treatment, depression, and hormonal dysregulation contributed to acute sarcopenia in elderly with COVID-19 patients. Acute sarcopenia contributes to a higher risk of immune dysregulation and cytokine storm, length of stay and hospital readmission, ICU admission and mechanical ventilation. These will contribute to increased mortality in sarcopenic elderly with COVID-19. Future studies regarding the effect of nutrition and physical training (exercise) on the outcome of COVID-19 will be beneficial in daily clinical practice. Pharmacological therapy or interventions with neuroelectrical muscular stimulation for the elderly whose exercise is contraindicated should be further studied in RCTs.

**AUTHORS CONTRIBUTION STATEMENT**

I Gusti Putu Suka Aryana: Originated the study, conceptualization, definition of intellectual content, literature search, manuscript preparation, manuscript editing, manuscript review, and corresponding author. Dian Daniella: Conceptualization, the definition of intellectual content, literature search, manuscript preparation, manuscript editing, and manuscript review. Raden Ayu Tuty Kuswardhani: Literature search, manuscript preparation, manuscript editing, and manuscript review. Siti Setiati: Literature search, manuscript preparation, manuscript editing, and manuscript review.

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**CONFLICT OF INTEREST**

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**ETHICS CONSIDERATION**

Not Applicable.

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**AUTHORS CONTRIBUTION**

All authors contributed equally in the writing of this article.
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