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Hypothesis

Sarcopenia: An underlying treatment target during the COVID-19 pandemic

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ABSTRACT

The role of skeletal muscle mass in modulating immune response and supporting metabolic stress has been increasingly confirmed. Patients with sarcopenia, characterized by reduced muscle mass and muscle strength, were reported to have poor immune response and metabolic stress when facing acute infection, major surgeries, and other attacks. Based on empirical data, patients with sarcopenia are speculated to have increased infection rates and dismal prognoses amid the current 2019 novel coronavirus disease (COVID-19) epidemic. COVID-19 infection also aggravates sarcopenia because of the increased muscle wasting caused by systemic inflammation and the reduced physical activity and inadequate nutrient intake caused by social isolation. Notably, the interventions targeting skeletal muscle are anticipated to break the vicious circle and benefit the treatment of both conditions. We recommend sarcopenia assessment for populations with advanced age, inactivity, chronic disease, cancers, and nutritional deficiency. Patients with sarcopenia and COVID-19 infection need intensive care and aggressive treatments. The provision of at-home physical activities together with protein supplementation is anticipated to reverse sarcopenia and promote the prevention and treatment of COVID-19. The recommended protocols on nutritional support and physical activities are provided in detail.

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associated with a poor response to immune-checkpoint inhibitors in non–small cell lung cancers [17]. A recent prospective study also confirmed the impaired immune response in patients with sarcopenia after esophageal surgery [10]. The main mechanism underlying impaired immunity in patients with sarcopenia refers to the abnormal myokines, such as interleukin (IL)-15, IL-17, and IL-6, which modulate the proliferation and function of both innate and adaptive immune cells [12]. Regarding the metabolic stress during the severe infection, skeletal muscle is catabolized to provide the immune system, liver, and gut with amino acids, especially glutamine [11,18]. Patients with sarcopenia have a decreased availability of such protein mobilization. We speculate that patients with sarcopenia respond poorly to the infection of SARS-CoV-2 because of the impaired immune potential and metabolic stress.

No study has investigated the relationship between sarcopenia and COVID-19. However, some indirect evidence partially supports the adverse impact of sarcopenia on the treatment of COVID-19. First, advanced age, chronic diseases, and cancers, which were important etiologies of sarcopenia, were widely confirmed as risk factors for COVID-19 infection and corresponding mortality [19–21]. Second, sarcopenia was confirmed to be associated with the incidence of both community-acquired pneumonia and in-hospital pneumonia, which could be analogized to the COVID-19 infection [15,16]. Furthermore, patients with sarcopenia had compromised respiratory muscle strength and respiratory function, which were detrimental in the treatment of severe pneumonia and acute respiratory distress syndrome [9]. Additionally, sarcopenia was demonstrated as a risk factor for aspiration pneumonia in the older-adult population because of the dysfunction of the swallowing muscles, which may exacerbate the condition of bedridden patients with SARS-CoV-2 infection [8]. Considering this evidence, patients with sarcopenia predictably has increased infection rates, greater disease severity, and elevated mortality rates during the COVID-19 pandemic.

Conversely, COVID-19 could be a risk factor for the incidence and progression of sarcopenia because of the reduced physical activity and inadequate protein intake caused by social isolation [22,23]. Both physical exercise and protein-based nutrients have been confirmed as crucial factors in preventing and reversing sarcopenia [3]. The reduced oral protein intake and inactivity predictably aggravate muscle depletion [24]. The inflammatory reaction caused by COVID-19, especially the cytokine storm of interferon-α, interferon-γ, IL-6, IL-12, tumor necrosis factor-α, C-reactive protein, and monocyte chemotactic protein-1 inter observed in severe infection, refers to the elevated metabolic stress and muscle catabolism [25,26]. Theoretically, the interaction between sarcopenia and COVID-19, as shown in Figure 1, could be bidirectional and may form a vicious circle. However, the interventions for sarcopenia are promising in breaking this cycle and benefit the treatment of both conditions.

The diagnosis of sarcopenia could be a vital problem during the pandemic because of the limitation of medical resources and the implementation of social isolation. Patients with advanced age, inactivity, chronic disease, cancers, and nutritional deficiency should be specifically targeted for sarcopenia assessment [5]. The sarcopenia diagnosis consensus established by the European and Asian Working Groups for Sarcopenia (i.e., the combination of decreased muscle strength, muscle mass, and physical status) should be introduced in patients with COVID-19 infection to achieve definite diagnosis and severity classification [3,4]. However, for the community population, the self-measurement of handgrip strength and calf circumference and the use of the SARC-F questionnaire (strength, assistance in walking, rising from a chair, climbing stairs, and falls) could be helpful to detect sarcopenia and permit dynamic surveillance [3,4,27].

Therapeutic approaches targeting skeletal muscle are anticipated to promote the treatment of COVID-19. Both communities and hospitals should be places for interventions. The role of moderate-intensity exercise in promoting immune function has been widely validated [28,29]. Physical activities, especially aerobic and resistance exercise, also enhance muscle protein synthesis by sensitizing muscle to insulin- or amino acid–mediated anabolic actions [30,31]. Protein support together with physical activity were reported to successfully promote the reservation of skeletal muscle mass [32,33]. The provision of protein intake accompanied by physical exercise is thus promising in promoting immune response and metabolic stress, benefiting the treatment of both sarcopenia and COVID-19 [12,24]. Detailed protocols on nutrition and exercise interventions are discussed below. Notably, patients with sarcopenia and COVID-19 infection should be alert to secondary bacterial infection, pneumonia deterioration, and respiratory failure. Aggressive therapies, including intensive care, antiviral and antibiotic use, and mechanical ventilation, should be planned in advance. Additionally, patients with sarcopenia who are bedridden should be monitored for aspiration during oral or enteral feeding [8]. Agents to promote motility, such as prokinetic medications (metoclopramide or erythromycin) could be administrated appropriately to reduce aspiration [34]. Since patients with sarcopenia were reported to respond effectively to pulmonary rehabilitation, this strategy may be introduced to patients with sarcopenia to promote the prognosis of COVID-19 [35].
Regarding nutritional management during the COVID-19 pandemic, a balanced nutritional formula with high-quality protein (meat, fish, dairy, and eggs, which are rich in leucine) is recommended to promote muscle synthesis [36,37]. The recommended protein intake increases with age, from 0.75 to 0.80 g/kg/d in healthy adults to 1.0 to 1.2 g/kg/d in healthy older adults [37–39]. For older-adult patients with definite sarcopenia or severe illness, a protein intake of 1.2 to 1.5 g/kg/d should be considered [39]. Increased protein intake (>1.2 g/kg/d) is advised for those people who are exercising and otherwise active [38]. Furthermore, an extra supplementation of protein (10–20 g/d) during the exercise interventions should be considered for reversing sarcopenic status [33,40]. For patients with sarcopenia and COVID-19 infection, nutrition support should fit the increased inflammation reaction and metabolic stress. A calorie support of 25 to 30 cal/kg/d with a protein support of 1.2 to 2.0 g/kg/d should be considered for cases of severe infection [34]. Higher protein support (>2.0 g/kg/d) should be considered for cytokine storm observed in severe COVID-19 infection [25,34]. Notably, the enteral nutrition is superior to the parenteral nutrition for patients who are critically ill [34]. The supplementation of leucine-enriched whey protein accompanied with vitamin D could be a good formula in promoting muscle wasting in patients with sarcopenia with severe infection [41,42]. All these nutritional supplements could be helpful, although the recommendations cannot be totally achieved.

Generally, personalized physical activity protocol is recommended during the COVID-19 pandemic. Considering the impaired motor activity in patients with sarcopenia, the physical exercise protocols proposed by Jimenez-Pavon et al. [43] for older adults during the COVID-19 quarantine could be rationally referred. A multicomponent exercise program including aerobic, resistance, balance, coordination, and mobility training exercises should be safe and tolerated. An aerobic exercise of 200 to 400 min/wk distributed among 5 to 7 d, with a minimum of 2 to 3 d/wk of resistance exercise is an appropriate exercise volume. A moderate intensity (40–60% heart rate reserve or 65–75% of maximal heart rate) is anticipated to enhance the protective role of the exercise [43]. Additionally, grouped exercises consisting of 5 min of warm-up, 5 min of strengthening exercises, 5 min of balance exercises, and 5 min of cooldown could be the ideal exercise formula considering its feasibility and effectiveness [33]. Both chair exercises (toe raise, heel raise, knee lift, knee extension, hip flexion, and lateral leg raise) and ankle weight exercises with extra weight are workable without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33]. High-intensity exercises that overcome gravity, such as the double-arm pull-downs, sit-to-stand without complicated materials [33].

In conclusion, during the COVID-19 pandemic, patients with sarcopenia predictably are at higher-than average risk of infection and have poorer prognosis. This article proposes, to our knowledge for the first time, a vicious circle of interactions between sarcopenia and COVID-19. Interventions targeting sarcopenia are anticipated to benefit the prevention and treatment of COVID-19. Based on the aforementioned discussions, we propose the following recommendations:

1) A balanced nutritional formula including adequate protein intake with regular physical exercise (aerobic and resistance) should be achieved to prevent the development of sarcopenia and promote the community prevention of COVID-19.

2) Older adults, especially those with inactivity, chronic diseases, cancers, and nutritional deficiencies, should be targeted for sarcopenia assessment and classification during the COVID-19 pandemic, and those with definite sarcopenia warrant extra protein support (10–20 g/d).

3) Patients with sarcopenia with SARS-CoV-2 infection could benefit from early introduction of high-quality protein (1.2–2.0 g/kg/d, leucine-enriched) support accompanied with subtle physical exercise, which helps promote immune response and metabolic stress.

4) Patients with sarcopenia with severe COVID-19 infection warrant aggressive treatments, including but not limited to the early administration of intensive care, antiviral and antibiotic use, and mechanical ventilation.

Considering that controlling the pandemic outbreaks could be a long struggle, we anticipate further studies to directly reveal the interaction between sarcopenia and COVID-19 and establish validated protocols to solve these issues.

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