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NARRATIVE REVIEW

Nutritional management of muscle mass loss in patients with Post-COVID-19 Syndrome: a scoping review

Manejo nutricional na perda de massa muscular em pacientes com a Síndrome Pós-COVID-19: uma revisão de escopo

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KEYWORDS
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Muscle Loss
Malnutrition
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Physical Exercise
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ABSTRACT

Post-Covid-19 Syndrome (PCS) is a condition that causes persistent symptoms and impacts nutritional status such as loss of muscle mass. The objective of this study was to review and map scientific evidence on nutritional management in the loss of muscle mass in patients with PCS. The scoping review protocol was prepared following the PRISMA-ScR guidelines. Review articles not written in English or those that included only hospitalized patients and pertained to conditions other than PCS were excluded. Data extraction followed the methodology outlined by the Cochrane Review Group. Of the 81 articles initially identified, only five met the inclusion criteria. The selected studies emphasized the importance of recovering muscle mass, higher protein and caloric intake, and physical strength exercises. Consequently, nutritional interventions aimed at mitigating muscle mass loss should prioritize strategies that increase caloric and protein consumption.

PALAVRAS-CHAVE
Síndrome Pós-COVID-19
Perda Muscular
Desnutrição
Desnutrição Energética-proteica
Terapia Nutricional
Exercício Físico
COVID-19

RESUMO

A Síndrome Pós-covid-19 (SPC) é uma condição que acarreta sintomas persistentes e impactam o estado nutricional, como a perda de massa. O objetivo deste estudo foi realizar revisão para mapear evidências científicas acerca do manejo nutricional na perda de massa muscular em pacientes com SPC. O protocolo da revisão de escopo foi elaborado de acordo com o PRISMA-ScR. Foram excluídos artigos de revisão que não estivessem em inglês ou português, que incluíssem apenas pacientes hospitalizados e com outras condições que não a SPC. Os dados foram extraídos com base no *Cochrane Review Group*. 81 artigos foram identificados e a amostra final incluiu cinco estudos. Para a recuperação da massa muscular, maior ingestão proteica, calórica e exercícios físicos de força foram descritos nos estudos. A intervenção nutricional para recuperar a perda de massa muscular deve considerar estratégias que visam o aumento do consumo calórico e proteico.

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INTRODUCTION

In March 2020, the World Health Organization (WHO) declared an outbreak caused by the SARS-CoV-2 virus, commonly known as Coronavirus disease 19 (COVID-19), as a public health emergency[1]. The disease primarily impacts the respiratory system, manifesting in a spectrum of symptoms from mild respiratory issues to severe acute respiratory complications and, in some cases, death[2].

In Brazil, up to December 2023, approximately 38 million confirmed cases were reported, with a recovery rate exceeding 98%[3]. However, despite the majority of infected individuals recovering, some individuals may experience persistent symptoms for an extended period[4-7]. These lingering symptoms include metabolic and physical dysfunctions, tiredness, muscle pain, ageusia, anosmia, weakness, fatigue, dizziness, insomnia, depression, anxiety, difficulty paying attention, tingling in the extremities, and loss of muscle mass and strength[4-7]. Individuals experiencing one or more of these symptoms for more than 12 weeks after infection without underlying health conditions are diagnosed with Post-COVID-19 Syndrome (PCS)[8-10].

Among the array of symptoms related to PCS, the loss of muscle mass and strength significantly impacts patientfunctionality[11]. Persistent inflammation stemming from infection, which is associated with inadequate calorie and protein intake, contributes to muscle catabolism, leading to the loss of muscle mass in PCS[11]. Martone et al.[11] identified a prevalence of sarcopenia of 19.5% among patients following SARS-CoV-2 infection.

Given the potential negative impact on clinical, nutritional condition, and quality of life, establishing a nutritional intervention focused on muscle recovery is imperative. However, there is no consensus regarding nutritional recommendations, and there is limited literature available on nutritional management in this context. Thus, this study aims to synthesize scientific evidence of nutritional management in patients with PCS experiencing muscle mass loss.

METHODS

The study protocol was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) guidelines, with the checklist completed before starting the literature search. Five consecutive steps were carried out: identification of the research question; search for relevant studies; study selection; data extraction; and grouping, summarizing and presenting results[12,13].

Search strategy

To develop the research question and search strategy, the population, concept, and context (PCC)[12] strategy was used. Therefore, studies were included in this scoping review: a) pertaining to the population: adult and elderly patients; b) concerning the concept: nutritional management for loss of muscle mass; and c) focusing on the context: Post-Covid-19 Syndrome. This structured approach aimed to answer the following question: "What constitutes effective nutritional management for the loss of muscle mass in adult and elderly patients with PCS?"

The searches were conducted independently by two reviewers in October 2022 and were updated in December 2023 using the PubMed and SciELO databases. The Medical Subject Headings (MeSH) and their Portuguese counterparts *Descritores em Ciências da Saúde* (DeCS) were consulted. The following descriptors were used: covid-19; Sarcopenia; Muscle loss; Diet; nutrition therapy; Muscle fatigue, muscular atrophy, protein-energy malnutrition, energy requirement, energy intake, post-covid, covid syndrome, post-covid-19, long covid, Post-acute covid-19 syndrome. Searches in the databases were conducted using keywords with the connecting terms AND and OR. The searches were restricted to the period from 2020 to 2023 because of the topic's specificity. In addition, manual searches were performed in the references of the included studies to identify further relevant research.

Eligibility criteria

The inclusion and exclusion criteria were defined before the initiation of the searches. Original articles published between 2020 and 2023, written in English or Portuguese, and focusing on PCS in adults or elderly individuals undergoing outpatient treatment for muscle mass loss were eligible for inclusion. Review articles in languages other than those mentioned above, hospitalized patients, and patients with conditions other than PCS were excluded.

Data extraction

The titles and abstracts of the identified articles were compiled in a specially designed spreadsheet. Duplicates were removed. Two independent reviewers (BTFN and HGSA) screened the articles by reviewing their titles and abstracts to identify relevant ones. Articles meeting the inclusion criteria were then assessed in full to determine the final review sample. Any discrepancies in the inclusion or exclusion of publications were resolved by consensus with two additional reviewers (SFM and MCFT). Data extraction was performed using the Cochrane Consumer and Communication Review Group form[14]. Information extracted from the articles included authorship, year of publication, origin, type of study, objective, sample characteristics and size, methods, and main results, which were used and qualitatively presented.

RESULTS

After conducting searches on various platforms and using manual methods, 81 studies were identified. Following the removal of 41 duplicate articles, 40 unique articles were screened on the basis of their titles and abstracts according to the inclusion criteria. Subsequently, 19 articles were excluded because they did not present elements that met the objective of this review. The remaining 21 articles underwent full-text assessment, leading to the exclusion of 16 articles. Ultimately, the final review sample comprised five articles (Figure 1).

Table 1 presents the main information of the articles included in this scoping review.

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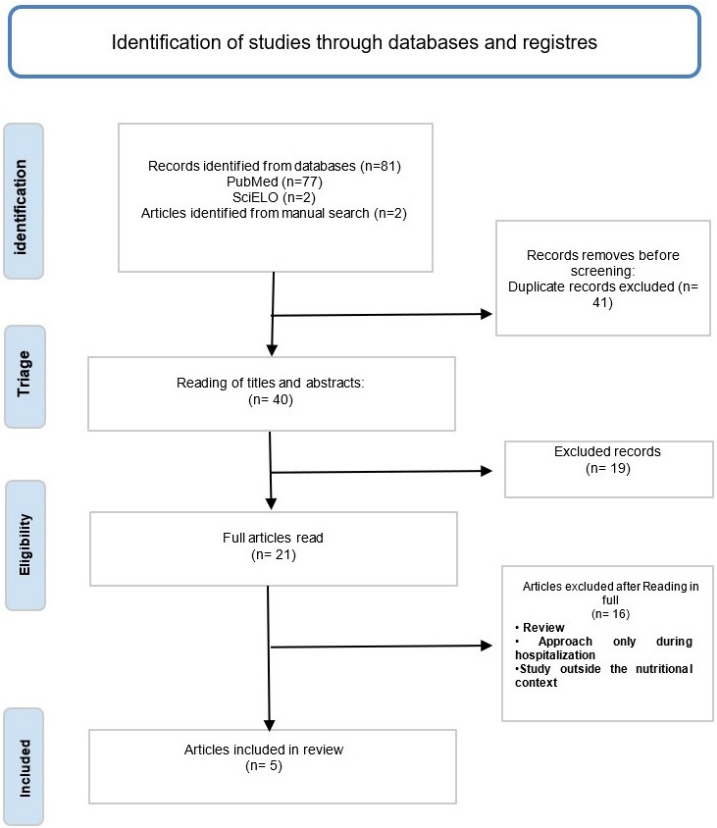

Figure 1 – PRISMA flowchart of nutritional management in muscle mass loss in outpatients with Post-Covid-19 Syndrome: a scoping review.

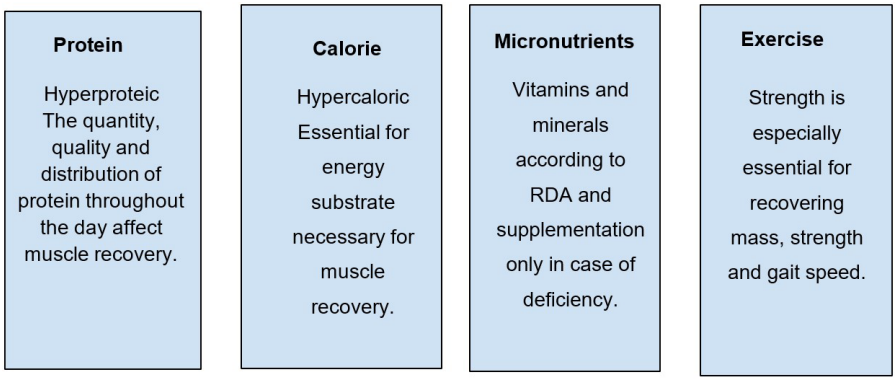

Figure 2 – Qualitative analysis of four themes from the results of the included studies.

Figure 2 presents the four themes constructed based on the qualitative analysis of the results of the studies included in this review[15-19].

DISCUSSION

Loss of muscle mass: concept, contextualization in PCS and relationship with nutritional status

The maintenance of muscle mass relies on a delicate balance between protein synthesis and degradation. Protein synthesis occurs through specific cellular signaling pathways, such as the mammalian target protein of rapamycin (mTOR) pathway, insulin-like growth factor type 1 (IGF-1) and insulin action. These pathways work together, binding to their receptors and ultimately stimulating protein synthesis[20,21]. In contrast, protein degradation primarily occurs through several intracellular pathways, including the ubiquitin-proteasome system and the autophagy-lysosomal system[20,21].When the rate of protein degradation surpasses that of synthesis, a process known as proteolysis, muscle mass is lost[21,22].

Table 1 – Extraction of data from articles selected for the scoping review.

Article title	Authors, year and country	Study design	Objectives	Population (n)	Methods	Results	Critical analysis/Conclusion
Impact of COVID-19 Infection and Persistent Lingering Symptoms on Patient Reported Indicators of Nutritional Risk and Malnutrition	Deer et al.[15], 2022, USA	Observational cohort	Determine dietary intake and nutrient distribution patterns in people after acute COVID-19 illness and with persistent symptoms.	Adults and elderly (n=92)	Nutritional assessment was carried out using subjective global assessment and 24-hour recall on 92 individuals in the post-covid-19 recovery clinic.	Patients at risk of malnutrition presented more symptoms (diarrhea, abdominal pain, loss of smell, loss of taste, congestion and dyspnea) in PCS. Less than 39% achieved the ideal protein intake of 1.2 g/kg/day proposed for recovery from muscle mass loss, according to American dietary guidelines. The distribution of proteins throughout the day was irregular; only 3% reached the recommendation for all meals, while more than 30% did not reach the recommendation for any meal.	This study has limitations due to the small sample, unable to stratify food consumption in relation to comorbidities and activity. The high risk of malnutrition in post-covid-19 patients stands out, requiring more detailed nutritional studies. The lack of compliance with nutritional recommendations is concerning, highlighting the need for better education and nutritional support to optimize post-infection recovery.
Long-Term Evolution of Malnutrition and Loss of Muscle Strength after COVID-19: A Major and Neglected Component of Long COVID-19	Gerard et al.[16], 2021, France	Prospective observational cohort	Assess weight loss and muscle dysfunction, in addition to persistent symptoms, 6 months after hospital discharge	Adults (n=288)	All patients discharged from hospital underwent teleconsultation 30 days after discharge. Patients received counseling diet, nutritional supplementation, adapted physical activity guidance or physiotherapeutic assistance. Six months after discharge, they were reevaluated. Muscle function, functional loss, and daily activity limitations were assessed using a standard screening tool during telehealth consultations. Nutritional status was assessed by the subjective global assessment produced by the patient.	Of the 119 participants monitored, 14.3% had decreased muscle strength and 36% had persistent malnutrition with inadequate protein and caloric intake according to AMDR.	The article presents limitations in relation to the teleconsultation evaluation and monitoring protocol and supplementation data and general guidelines. Subjective assessment of muscle strength has advantages and challenges. While it allows for long-term assessment without reference to prior level of strength, its objectivity is debated. Post-COVID management must prioritize nutritional support and rehabilitation to prevent long-term disability and sarcopenia. Identifying patients on atypical recovery trajectories can direct additional interventions, especially for obese patients and those in intensive care.
Nutritional status in post SARS-CoV2 rehabilitation patients	Gobbi et al.[17], 2022, Italy	Observational	To evaluate the presence of malnutrition in patients with PCS and the effects of a multidisciplinary rehabilitation program on nutritional and functional status.	Elderly (n=48)	48 patients were evaluated after admission to a 3 to 4 week rehabilitation program with progressive resistance and aerobic physical exercises and nutritional intervention with caloric intake of 27 to 30 kcal/kg per day and 1 to 1.3g/kg of protein per day. day. Body composition (bioimpedance), physical performance and muscle strength (manual pressure test and TUG) were evaluated at admission and discharge from the program.	According to the Global Leadership Initiative on Malnutrition criteria, 60% were malnourished before entering the rehabilitation program. After the program there was an improvement in nutritional and physical status, a significant increase (p=0.001) in the appendicular skeletal muscle index in females from 5.2 to 5.8 kg/m^2, a significant increase (p=0.014) in muscle strength in male from 23.3 to 26.7kgf. Body weight did not change significantly. A reduction in TUG test values was observed from 25.4 to 15.9.	A study with sample limitations and lack of measurements of inflammatory markers suggests the need for confirmation by larger studies, however it indicates that personalized nutritional interventions can improve the nutritional and functional status of patients.

Note: g = gram; kg = kilogram; AMDR = Acceptable Macronutrient Distribution Ranges; TUG = Timed Up and Go; m^2 = square meter; kgf = kilogram-force; Kcal = Kilocalorie.

Table 1 – Continued...

Article title	Authors, year and country	Study design	Objectives	Population (n)	Methods	Results	Critical analysis/Conclusion
Observational study on the benefit of a nutritional supplement, supporting immune function and energy metabolism, on chronic fatigue associated with the SARS-CoV-2 post-infection progress	Rossato et al.[18], 2021, Italy	Observational	Evaluate the response to a supplement with vitamins, minerals and amino acids in improving chronic fatigue in patients with PCS	Adults (n=201)	201 participants who had persistent fatigue in PCS were included. Everyone received one unit per day (5.5g/day sachet) of the Apportal® supplement (vitamins, minerals, arginine, carnitine, plant extracts such as Panax Ginseng and Eleutherococcus Senticosus, coenzyme Q10 and lycopene) for 28 days and were re-evaluated by questionnaires at the 14th and 28th days in relation to general fatigue, mental fatigue and quality of life.	Patients achieved significant improvements in assessments of chronic fatigue and quality of life. On the 14th day there was an improvement of 76.62% in fatigue and quality of life and on the 28th day an improvement of 90.05%.	The study does not present a control group or biochemical analysis. In conclusion, it suggests a potentially effective solution for reducing chronic fatigue and improving quality of life.
Skeletal Muscle Mass, Sarcopenia and Rehabilitation Outcomes in Post-Acute COVID-19 Patients	Gobbi et al.[19], 2021, Italy	Prospective	To investigate the impact of sarcopenia in a rehabilitation unit for patients with PCS on body composition, functional and respiratory capacity.	Elderly (n=34)	34 patients underwent a physical assessment and were separated into sarcopenic and non-sarcopenic groups. Physical exercises and nutritional intervention were performed with intake of 27 to 30 kcal/kg of adjusted weight, 1 to 1.3g/kg of protein per day, fat and carbohydrate ratio 30:70 or 50:50. They also received essential amino acids of 4 to 8g per day, multiminerals (K, Ca, P, Mg, Mn, Mo, Se, Cr, I, Fe, Zn, Cu) and multivitamins vitamin A, B, D, E, C, K. Vitamin D being 1000 IU/day, or 10000 IU per week or 25,000 IU/2 weeks or 50,000 IU/4 weeks.	There was an improvement in the parameters of body composition, muscle strength and functional capacity in sarcopenic (p=0.001) and non-sarcopenic (p=0.009) patients. Rehabilitation, in particular strength training in these patients, is crucial for the recovery of functional independence.	The study has a limited sample. However, it highlights the importance of monitoring muscle mass and strength in post-COVID-19 patients. Rehabilitation, including resistance training, is crucial to regaining independence. Personalized rehabilitation protocols, integrated with nutritional interventions, are essential.

Note: g = gram; kg = kilogram; AMDR = Acceptable Macronutrient Distribution Ranges; TUG = Timed Up and Go; m^2 = square meter; kgf = kilogram-force; Kcal = Kilocalorie.

Sarcopenia, as defined by the criteria of the European Working Group on Sarcopenia in Older People 2 (EWGSOP 2), is characterized by the simultaneous loss of muscle mass and strength[23,24]. This condition is classified as primary when it occurs in association with aging and as secondary when it results from factors such as a sedentary lifestyle, malnutrition, or underlying diseases. Prolonged hospitalization, for instance, can contribute to muscle mass and strength loss due to decreased muscle use, a situation intensified by concurrent inflammatory processes[19,22-26].

COVID-19 is a disease that induces the loss of muscle mass and strength. Common symptoms of the infection, such as ageusia, anosmia, and loss of appetite, can contribute to weight loss and malnutrition[5,7,27-29]. In addition, decreased physical activity, lower food intake, and inflammation accelerate the loss of muscle mass[5,27,28,30]. SARS-CoV-2 infection can trigger severe inflammation, particularly in patients in the acute phase of the disease. This inflammation contributes to increased proteolysis, disrupts metabolic homeostasis, and exacerbates muscle catabolism. Consequently, the combination of muscle loss, inflammation, and reduced caloric and protein intake leads to a high prevalence of malnutrition and sarcopenia in these patients[15,31-34].

Individuals with PCS may continue to experience or develop loss of muscle mass due to various factors, including sustained systemic inflammation, reduced food intake, and physical inactivity. Persistent systemic inflammation can increase energy demands, worsening protein degradation as dietary intake often fails to meet the increased requirements[15,31,33]. The resulting loss of muscle mass and strength can compromise functionality, increase the risk of falls, impair immunity, and increase mortality rates, particularly among the elderly, in addition to worsening quality of life[35,36].

Gérard et al.[16] evaluated 288 patients 30 days after hospital discharge due to COVID-19. Patients had marked weight loss and/or muscle dysfunction with a performance status of >2, as assessed through self-assessment of muscle function using verbal and nonverbal analog scales. The authors reassessed them after 6 months to determine nutritional status, evolution of muscle strength, physical/functional performance status, and persistent symptoms such as fatigue, dyspnea, depression, and anxiety. It was observed that the group of patients who presented the most compromised nutritional status after 6 months were individuals who had been in intensive care and those with obesity. These individuals also had a higher risk of functional loss. Furthermore, after 6 months of follow-up, 15% of the cohort still had malnutrition even after nutritional intervention[16]. It is important to highlight that the criteria for malnutrition (considering a phenotypic and an etiological criterion) are essential for a more comprehensive diagnosis of this condition, not being based solely on body mass index (BMI)[19,25,37].

According to Martone et al.[11] and Gérard et al.[16], sarcopenic patients exhibited a higher average number of symptoms following COVID-19 than non-sarcopenic patients, thereby influencing the prognosis and exacerbating nutritional status post-COVID-19. The prevalence of sarcopenia was elevated, particularly among individuals who underwent invasive mechanical ventilation (IMV) during hospitalization. Moreover, prolonged hospitalization was associated with an increased risk of PCS and sarcopenia[29].

Other risk factors for loss of muscle mass in PCS include advanced age, immobility, inadequate nutrition, inflammation, malnutrition, and obesity[15,16,19,22,38]. Individuals diagnosed with obesity when infected with SARS-CoV-2 face a heightened risk of developing sarcopenia post-infection because the pro-inflammatory state of obesity can increase muscle catabolism and inhibit anabolism pathways leading to sarcopenic obesity[5,32,39]. Therefore, individuals with obesity and PCS deserve special attention[16,40,41].

Furthermore, the elderly population exhibits reduced stimulation of muscle protein synthesis in response to physical exercise and protein intake. Therefore, they are less responsive to the anabolic effects of exercise and dietary proteins and essential amino acids, thereby increasing the risk of sarcopenia in PCS. To counteract this, older individuals require a higher daily protein intake and adequate calorie consumption[27,42]. Nutritional status before infection and pre-existing diseases are also risk factors for the development of PCS[15,16,19,22,30].

Therefore, a multidisciplinary approach is necessary to improve the clinical picture of muscle mass loss using adequate nutritional management, inflammation control, physical exercise, and muscle strengthening[5,11].

Nutritional management for the loss of muscle mass

Adequate intake of calories, protein, and essential micronutrients contributes to the functioning of the immune system, especially after an excessive release of pro-inflammatory cytokines that occurs during infection[15], which includes an inflammatory response with an increase in tumor necrosis factor alpha (TNF-α) and Interleukin-6 (IL-6). This acute inflammation is associated with the loss of muscle mass and the development of sarcopenia[5,43]. Therefore, nutritional management is important for controlling symptoms arising from inflammation and persistent PCS. The caloric supply must meet the energy expenditure of individuals, seeking to stop the breakdown of muscle proteins to generate energy.

In this context, muscle recovery requires a high-calorie, high-protein diet. Protein is a primary macronutrient crucial for enhancing the nutritional and functional status of patients[30]. Insufficient protein intake is directly linked to muscle mass loss, primarily because of reduced muscle protein synthesis[23]. Furthermore, the significance of essential fatty acids, carbohydrates, and vitamin D in the recovery of muscle mass has been highlighted[11,30].

Because of the characteristics of PCS, the consumption of foods known for their anti-inflammatory and immunostimulating activities should be encouraged[30]. The dietary pattern of the Mediterranean diet includes these characteristics in addition to antioxidant components[30,44]. Papadopoulou et al.[45] carried out a review with the aim of investigating an association between the Mediterranean diet and the prevention and/or improvement of sarcopenia in the elderly. Their findings indicate a positive effect of adhering to the Mediterranean diet on muscle mass,

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although conclusive evidence regarding its effects on muscle strength was not identified[45].

Food intake in adequate caloric amounts is necessary to reduce exacerbated muscle catabolism and the risk of protein-energy malnutrition[15]. Gobbi et al.[17] carried out a nutritional intervention in patients with PCS lasting 3–4 weeks. Caloric intake ranged from 27 to 30 kcal/kg per day using adjusted body weight. Multivitamin and mineral supplementation, carnitine, and probiotics were administered in addition to a high-protein diet and physical exercise. After the intervention, participants achieved significant improvements in muscle strength and body composition by bioelectrical impedance analysis (BIA) and better physical performance as assessed by timed up and go (TUG)[17].

Hoyois et al.[41] investigated the impact of a nutritional intervention on the recovery of patients following acute COVID-19 infection, with an energy intake of 30 kcal/kg/day and protein supplementation ranging from 1 to 1.6 g/kg/day via oral means. After the intervention, participants demonstrated a significant increase in average weight by 4.3 kg (2.7-6.7 kg), and the average handgrip strength increased significantly by up to 64.7%[41]. According to the European Society of Parenteral and Enteral Nutrition (ESPEN), the use of oral supplements may be indicated, especially when nutritional needs are not being met[46]. It is worth noting that meeting caloric needs in patients with PCS can be challenging because these patients usually present a series of symptoms that compromise regular food consumption, such as ageusia and anosmia[5,46].

Protein supply

The nutritional approach most used in the management of PCS according to the studies analyzed was the consumption of proteins. The importance of protein in nutritional management in the context of loss of muscle mass and sarcopenia is known[5,23,27,35]. Protein synthesis is stimulated by protein intake; in addition, protein stimulates insulin, which reduces proteolysis and increases the anabolic response[42]. Gobbi et al.[17] investigated the consumption of 1–1.3 g/kg of protein per day in individuals with PCS. When oral protein intake was not sufficient, supplementation based on whey protein or vegetable proteins was used to achieve the necessary daily protein target. The authors found an increase in muscle mass in female individuals (p=0.001), although there were no significant changes in body weight. There was a significant improvement in phase angle (Pha) values, an increase in muscle strength in men, and an improvement in physical performance observed by the reduction in TUG[17] values. In another study by Gobbi et al.[19], the impact of a high-protein diet for 28 days (1 to 1.3 g/kg of protein per day) on individuals with PCS was investigated. An improvement of 19.71% in handgrip strength was observed after the intervention[19]. In this context, an increase in protein intake in patients with PCS[30] is suggested.

The Society of Sarcopenia, Cachexia and Disorders (SCWD) recommends protein intake together with resistance exercise as the primary treatment strategy for combating sarcopenia[47]. SCWD also recommends 1-1.5 g/kg of protein per day for the management of muscle mass loss when these individuals are in proinflammatory states, as occurs in PCS. It is worth noting that the recommendation can reach up to 2 g/kg per day of protein[43,47]. The ESPEN 2020 guidelines for COVID-19 in the acute phase advise approximately 27–30 kcal/kg per day and 1.2-1.5 g/kg per day of protein for adequate recovery of muscle mass[46].

Nistor-Cseppento et al.[22] conducted a case–control study with patients with PCS, wherein one group received a high-protein diet and probiotics, while the other group served as a control and did not receive these interventions. Both groups received vitamin D supplements and engaged in physical exercise for 2 months. The eating plan consisted of three main meals and two snacks per day. The experimental group received 1.2-1.5 g/kg/day of protein and the control group 0.8 g/kg/day. The meals consisted of meat, eggs, dairy products, rice, beans, and food rich in leucine, prioritizing essential proteins. Nutritional monitoring was performed weekly and nutritional assessment was performed monthly for 2 months.The intervention group achieved a significant improvement in muscle mass index (SMI) values from 6.7 to 6.92 ± 0.50 kg/ m^2 and the control group from 6.5 to 6.77 ± 0.56 kg/ m^2. At the end of the approach, there was a reduction in the number of patients with sarcopenia from 80.64% to 34.57%, in addition to an increase in SMI values from 19.35% to 65.42%. Therefore, it was concluded that eating a high-protein diet reduced the loss of muscle mass by 40%[22].

Deer et al.[15] evaluated the food consumption of individuals with PCS. Participants had an average daily consumption of 1,707.8 ± 720.3 kcal per day, ranging from 178.9 to 4,443.3 kcal. A high prevalence of malnutrition was found (48%), and they had more post-covid-19 symptoms such as diarrhea and loss of smell and taste. Consumption was adjusted to 1.2 g/kg of protein per day and a limit of 0.4 g/kg of protein per meal. Participants had a daily consumption significantly lower than proposed, being 0.8 ± 0.4 g/kg and consumption per ideal body weight 0.98 ± 0.5 g/kg greater than the recommended daily intake (RDA). Only 31.5% and 8.7% of the participants managed to reach 0.4 g/kg of protein at lunch and breakfast, respectively. The majority (52.2%) reached the threshold at dinner. Less than 40% of individuals reached the recommendation of 1.2 g/kg of protein per day, in addition to low consumption of fruits and vegetables. It is worth noting that this study did not evaluate eating habits before SARS-CoV-2[15] infection.

The significance of protein consumption in muscle recovery is evident, with both the daily amount and its distribution throughout the day being key factors for better results[15]. According to the studies included in this review, improvement in muscle mass loss was associated with adequate protein consumption, vitamin D at optimal levels, and essential amino acids, contributing to metabolic homeostasis, reduced proteolysis, and increased anabolism[11,19].

Use of nutritional supplements

Vitamins and minerals play an important role in the body as cofactors in various metabolic mechanisms, including neutralizing physical fatigue. The vitamin C and B complex

and minerals such as iron and magnesium contribute to recovery from fatigue. In this sense, Rossato et al.[18] analyzed the benefits of daily supplementation with a sachet of ApportAL® (vitamins, minerals, arginine, carnitine, plant extracts such as Panax Ginseng and Eleutherococcus Senticosus, coenzyme Q10 and lycopene) for 14 and 28 days in fatigue chronic history of individuals with PCS (n = 201) through self-administered questionnaires. The study found positive results (improvement in chronic fatigue and quality of life); however, the authors suggest conducting a study with a control group to analyze whether the improvement obtained was really due to the use of supplementation or whether the same would occur with time, in addition to using more reliable parameters to evaluate instead of self-administered questionnaires[18].

The ESPEN Guidelines for COVID-19 recommend the intake of 100% of the RDA for those who are malnourished and supplementation for those who are deficient in any micronutrient[46]. Some preliminary studies suggest that deficiency of nutrients such as vitamin C, B vitamins, magnesium, essential fatty acids, zinc, l-tryptophan, l-carnitine, and coenzyme Q10, by increasing oxidative stress, may contribute to greater severity and progression. of the symptoms of PCS[48].

It is worth highlighting that the intestinal microbiota influences the absorption of nutrients and the control of inflammation. The state of intensified inflammation caused by SARS-CoV-2 infection leads to increased intestinal permeability, which can trigger reduced absorption of nutrients and thus further increase catabolism, along with common symptoms that make food intake difficult[5,22]. Some studies associate changes in the intestinal microbiota (due to the use of antibiotics and inflammation from COVID-19)[48,49] with the occurrence and severity of PCS[48]. In this context, the use of probiotics could contribute to a balanced intestinal microbiota and consequently a better general homeostasis of the organism[27].

Nistor-Csappento et al.[22] carried out a study with individuals with PCS who presented sarcopenia (n=200). The experimental group received nutritional intervention for 2 months, consisting of a high-protein diet (1.2-1.5 g/kg of protein) and probiotics (4 g sachet of standardized nutritional supplement containing 6 bacterial strains: *Enterococcus faecium*, *Lactobacillus acidophilus*, *L. brevis*, *Lactococcus lactis*, *Bifidobacterium bifidum* and *B. lactis*). Both groups, control and experimental, practiced physical exercises in addition to receiving 2,000 IU vitamin D supplementation with the aim of promoting an improvement in the function of mitochondrial oxidative phosphorylation in skeletal muscle, which is responsible for energy production in this tissue. The experimental group demonstrated significant improvements compared with the control group, including a higher skeletal muscle mass index ($p<0.048$) and lower prevalence of sarcopenia ($p<0.001$)[22].

Gobbi et al.[19] studied individuals with sarcopenic PCS and subjected to nutritional intervention with proteins, micronutrients, and training. Patients were supplemented with oral multimineral compounds (K, Ca, P, Mg, Mn, Mo, Se, Cr, I, Fe, Zn, Cu), in addition to 4–8 g of essential amino acids and multivitamins (vitamins A, B, C, D, E and K). The vitamin D dosage was 1,000 IU/day, 10,000 IU/week, 25,000 IU/2 weeks, and 50,000 IU/4 weeks. The authors observed improvements in muscle strength, physical performance, and body composition during 3–4 weeks of nutritional treatment in the sarcopenic group[19].

Vitamin D plays a pivotal role in supporting the immune system by reducing the concentrations of proinflammatory cytokines and increasing the levels of angiotensin-converting enzyme 2 (ACE2)[48]. Given its importance, the Clinical Guideline of the Endocrinology Society and ESPEN recommend that patients consume 100% of the RDA, and if they are deficient, supplementation is recommended[46,50,51]. Therefore, vitamin D supplementation in individuals with PCS who are deficient in this vitamin may be necessary and provide benefits. In this sense, some evidence suggests that vitamin D supplementation in individuals with deficiency can have a positive impact on the recovery of muscle strength[5,47].

Physical exercises to recover muscle mass

In addition to the nutritional strategies examined in this review, physical exercise is fundamental for recovering muscle mass[27,43]. Physical exercise is recommended for treating sarcopenia according to the International Clinical Practice Guidelines for Sarcopenia (ICFSR)[24]. Specifically, resistance exercise stands out for its ability to enhance muscle mass, muscle strength, and physical performance[35,47]. Muscle protein synthesis is stimulated by physical exercise, with a significant increase observed during resistance training protocols[27]. Furthermore, there is an association between resistance physical exercise and a lower incidence of sarcopenia; therefore, physical inactivity, a common condition in patients with PCS, can contribute to the loss of muscle mass[22,36,43]. In this sense, in addition to adequate caloric and protein intake, physical exercise should be part of the treatment to recover muscle mass[11,27].

The articles included in this review mostly used muscular resistance exercises[17,19] with the objective of gaining strength and muscular hypertrophy, in addition to aerobic exercises[17] to gain cardiovascular resistance and improve gait speed. In a study by Hoyois et al.[41], one of the proposed interventions was resistance physical exercise in patients after acute COVID-19 infection, which consisted of 90-min daily sessions in addition to nutritional counseling, psychosocial support, and occupational therapy. To assess functionality, a 2-min walking test was performed before treatments and another after.After 2 months of the approach, there was a significant improvement in muscle strength from 19% to 64.7% and a weight gain of 4.3 kg[41].

Gobbi et al.[19] conducted a study with post-covid-19 malnourished individuals (n=48), subjecting them to a nutritional intervention that included protein intake, micronutrients, and physical training. In his approach, exercises were used to improve conditioning, such as three sets of sitting down and getting up in bed, with 8–12 repetitions. Aerobic exercises were gradually introduced using an arm cycle ergometer at 65% of the maximum heart rate (MHR). Training targeted 45 min per session, six times a week, for 25 days. After the intervention,

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there was a significant improvement of 19.71% in handgrip strength (p=0.007)[19].

In the intervention by Nistor-Cseppento et al.[22], with outpatients, both the control group (n=107) and the experimental group (n=93) participated in physical exercise sessions lasting 40 min, consisting of 10 min of stretching and 20 min of resistance exercises, reaching up to 70% of MHR. After 2 months, both groups achieved improvements in the skeletal muscle index, but the experimental group, which received nutritional therapy with protein and probiotics in addition to physical exercise and vitamin D supplementation, achieved better results and fewer individuals with sarcopenia (75% with sarcopenia at the beginning vs. 37% with sarcopenia at the end, p<0.001)[22]. These findings indicate that the recovery of muscle mass requires a set of nutritional interventions, especially caloric and protein, associated with resistance physical exercise[22].

This review presents some limitations that must be considered. First, few studies have evaluated nutritional intervention in PCS. In addition, the studies are heterogeneous in terms of sample sizes and varied nutritional interventions. This makes comparisons between studies difficult. It is also important to highlight that the studies included were conducted only in the outpatient context. Furthermore, only studies in English and Portuguese were considered, which may have resulted in the exclusion of important evidence available in other languages. Therefore, the need for new studies evaluating the nutritional status of patients with PCS and adequate nutritional management is emphasized.

CONCLUSION

Hyperproteic and hypercaloric nutritional intervention is necessary for the nutritional management of patients with PCS experiencing muscle mass and strength loss. Furthermore, the importance of adequate intake of vitamins and minerals in a global recovery context was also noted, as was the inclusion of regular physical exercise in patients with PCS. More studies on the subject, especially case-control studies, are necessary to deepen our knowledge.

REFERÊNCIAS

1. World Health Organization. Director General's Opening remarks at the media briefing on COVID-19 [Internet]. Geneva: WHO; 2020 [cited 2023 May 10]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
2. Umakanthan S, Sahu P, Ranade AV, Bukelo MM, Rao JS, Abrahao-Machado LF, et al. Origin, transmission, diagnosis and management of coronavirus disease 2019 (COVID-19). Postgrad Med J. 2020;96(1142):753-8. http://doi.org/10.1136/postgradmedj-2020-138234. PMid:32563999.
3. Brasil. Ministério da Saúde. Coronavírus Brasil: painel geral [Internet]. Brasília; 2020 [cited 2023 May 16]. Available from: https://covid.saude.gov.br
4. Augustin M, Schommers P, Stecher M, Dewald F, Gieselmann L, Gruell H, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. The Lancet Regional Health-Europe. 2021;6:100122. http://doi.org/10.1016/j.lanepe.2021.100122. PMid:34027514.
5. Piotrowicz K, Gąsowski J, Michel JP, Veronese N. Post-COVID-19 acute sarcopenia: physiopathology and management. Aging Clin Exp Res. 2021;33(10):2887-98. http://doi.org/10.1007/s40520-021-01942-8. PMid:34328636.
6. Crispo A, Bimonte S, Porciello G, Forte CA, Cuomo G, Montagnese C, et al. Strategies to evaluate outcomes in long-COVID-19 and post-COVID survivors. Infect Agent Cancer. 2021;16(1):62. http://doi.org/10.1186/s13027-021-00401-3. PMid:34717691.
7. Cha C, Baek G. Symptoms and management of long COVID: a scoping review. J Clin Nurs. 2024;33(1):11-28. http://doi.org/10.1111/jocn.16150. PMid:34913540.
8. Scholkmann F, May C-A. COVID-19, post-acute COVID-19 syndrome (PACS,"long COVID") and post-COVID-19 vaccination syndrome (PCVS,"post-COVIDvac-syndrome"): similarities and differences. Pathol Res Pract. 2023;246:154497. http://doi.org/10.1016/j.prp.2023.154497. PMid:37192595.
9. Sandler CX, Wyller VB, Moss-Morris R, Buchwald D, Crawley E, Hautvast J, et al. Long COVID and post-infective fatigue syndrome: a review. Open Forum Infect Dis. 2021;8(10):ofab440. http://doi.org/10.1093/ofid/ofab440. PMid:34631916.
10. Rodriguez-Sanchez I, Rodriguez-Manãs L, Laosa O. Long COVID-19: the need for an interdisciplinary approach. Clin Res Rev. 2021;15(3):869-75. http://doi.org/10.1016/j.cger.2022.03.005.
11. Martone AM, Tosato M, Ciciarello F, Galluzzo V, Zazzara MB, Pais C, et al. Sarcopenia as a potential biological substrate of long COVID-19 syndrome: prevalence, clinical features, and risk factors. J Cachexia Sarcopenia Muscle. 2022;13(4):1974-82. http://doi.org/10.1002/jcsm.12931. PMid:35698920.
12. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005;8(1):19-32. http://doi.org/10.1080/1364557032000119616.
13. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci. 2010;5(1):69. http://doi.org/10.1186/1748-5908-5-69. PMid:20854677.
14. Cochrane Consumers and Communication. Data extraction template for included studies. Victoria: Cochrane; 2016. 25 p.
15. Deer RR, Hosein E, Harvey M, Nguyen T, Givan A, Hamilton M, et al. Impact of COVID-19 infection and persistent lingering symptoms on patient reported indicators of nutritional risk and malnutrition. Nutrients. 2022;14(3):642. http://doi.org/10.3390/nu14030642. PMid:35277001.
16. Gérard M, Mahmutovic M, Malgras A, Michot N, Scheyer N, Jaussaud R, et al. Long-term evolution of malnutrition and loss of muscle strength after COVID-19: a major and neglected component of long COVID-19. Nutrients. 2021;13(11):3964. http://doi.org/10.3390/nu13113964. PMid:34836219.
17. Gobbi M, Brunani A, Arreghini M, Baccalaro G, Dellepiane D, La Vela V, et al. Nutritional status in post SARS-Cov2 rehabilitation patients. Clin Nutr. 2022;41(12):3055-60. http://doi.org/10.1016/j.clnu.2021.04.013. PMid:34049750.
18. Rossato MS, Brilli E, Ferri N, Giordano G, Tarantino G. Observational study on the benefit of a nutritional supplement, supporting immune function and energy metabolism, on chronic fatigue associated with the SARS-CoV-2 post-infection progress. Clin Nutr ESPEN. 2021;46:510-8. http://doi.org/10.1016/j.clnesp.2021.08.031. PMid:34857243.
19. Gobbi M, Bezzoli E, Ismelli F, Trotti G, Cortellezzi S, Meneguzzo F, et al. Skeletal muscle mass, sarcopenia and rehabilitation outcomes in post-acute COVID-19 patients. J Clin Med. 2021;10(23):5623. http://doi.org/10.3390/jcm10235623. PMid:34884325.

20. Peris-Moreno D, Cussonneau L, Combaret L, Polge C, Taillandier D. Ubiquitin ligases at the heart of skeletal muscle atrophy control. Molecules. 2021;26(2):407. http://doi.org/10.3390/molecules26020407. PMid:33466753.

21. Vainshtein A, Sandri M. Signaling pathways that control muscle mass. Int J Mol Sci. 2020;21(13):4759. http://doi.org/10.3390/ijms21134759. PMid:32635462.

22. Nistor-Cseppento CD, Moga TD, Bungau AF, Tit DM, Negrut N, Pasca B, et al. The contribution of diet therapy and probiotics in the treatment of sarcopenia induced by prolonged immobilization caused by the COVID-19 pandemic. Nutrients. 2022;14(21):4701. http://doi.org/10.3390/nu14214701. PMid:36364963.

23. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31. http://doi.org/10.1093/ageing/afy169. PMid:30312372.

24. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, et al. International clinical practice guidelines for sarcopenia (ICFSR): screening, diagnosis and management. J Nutr Health Aging. 2018;22(10):1148-61. http://doi.org/10.1007/s12603-018-1139-9. PMid:30498820.

25. González-Islas D, Sánchez-Moreno C, Orea-Tejeda A, Hernández-López S, Salgado-Fernández F, Keirns-Davis C, et al. Body composition and risk factors associated with sarcopenia in post-COVID patients after moderate or severe COVID-19 infections. BMC Pulm Med. 2022;22(1):223. http://doi.org/10.1186/s12890-022-02014-x. PMid:35676657.

26. Morley JE, Kalantar-Zadeh K, Anker SD. COVID-19: a major cause of cachexia and sarcopenia? J Cachexia Sarcopenia Muscle. 2020;11(4):863-5. http://doi.org/10.1002/jcsm.12589. PMid:32519505.

27. Rogeri PS, Zanella R Jr, Martins GL, Garcia MD, Leite G, Lugaresi R, et al. Strategies to prevent sarcopenia in the aging process: role of protein intake and exercise. Nutrients. 2021;14(1):52. http://doi.org/10.3390/nu14010052. PMid:35010928.

28. Di Filippo L, De Lorenzo R, D'Amico M, Sofia V, Roveri L, Mele R, et al. COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalization: a post-hoc analysis of a prospective cohort study. Clin Nutr. 2021;40(4):2420-6. http://doi.org/10.1016/j.clnu.2020.10.043. PMid:33160700.

29. Akbarialiabad H, Taghrir MH, Abdollahi A, Ghahramani N, Kumar M, Paydar S, et al. Long COVID, a comprehensive systematic scoping review. Infection. 2021;49(6):1163. http://doi.org/10.1007/s15010-021-01666-x. PMid:34319569.

30. Barrea L, Grant WB, Frias-Toral E, Vetrani C, Verde L, de Alteriis G, et al. Dietary recommendations for post-COVID-19 syndrome. Nutrients. 2022;14(6):1305. http://doi.org/10.3390/nu14061305. PMid:35334962.

31. Ghanem J, Passadori A, Severac F, Dieterlen A, Geny B, Andrès E. Effects of Rehabilitation on Long-COVID-19 Patient's Autonomy, Symptoms and Nutritional Observance. Nutrients. 2022;14(15):3027. http://doi.org/10.3390/nu14153027. PMid:35893881.

32. Choi KM. Sarcopenia and sarcopenic obesity. Korean J Intern Med. 2016;31(6):1054-60. http://doi.org/10.3904/kjim.2016.193. PMid:27809450.

33. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the Cytokine Storm in COVID-19. J Infect. 2020;80(6):607-13. http://doi.org/10.1016/j.jinf.2020.03.037. PMid:32283152.

34. Anker MS, Landmesser U, von Haehling S, Butler J, Coats AJ, Anker SD. Weight loss, malnutrition, and cachexia in COVID-19: facts and numbers. J Cachexia Sarcopenia Muscle. 2021;12(1):9-13. http://doi.org/10.1002/jcsm.12674. PMid:33382211.

35. Wang Y, Tan S, Yan Q, Gao Y. Sarcopenia and COVID-19 outcomes. Clin Interv Aging. 2023;18:359-73. http://doi.org/10.2147/CIA.S398386. PMid:36923269.

36. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31. http://doi.org/10.1093/ageing/afy169. PMid:30312372.

37. Vaillant MF, Agier L, Martineau C, Philipponneau M, Romand D, Masdoua V, et al. Food intake and weight loss of surviving inpatients in the course of COVID-19 infection: A longitudinal study of the multicenter NutriCoviD30 cohort. Nutrition. 2022;93:111433. http://doi.org/10.1016/j.nut.2021.111433. PMid:34482098.

38. Thoma A, Akter-Miah T, Reade RL, Lightfoot AP. Targeting reactive oxygen species (ROS) to combat the age-related loss of muscle mass and function. Biogerontology. 2020;21(4):475-84. http://doi.org/10.1007/s10522-020-09883-x. PMid:32447556.

39. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA, et al. Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. Obes Facts. 2022;15(3):321-35. http://doi.org/10.1159/000521241. PMid:35196654.

40. Gualtieri P, Falcone C, Romano L, Macheda S, Correale P, Arciello P, et al. Body composition findings by computed tomography in SARS-CoV-2 patients: increased risk of muscle wasting in obesity. Int J Mol Sci. 2020;21(13):4670. http://doi.org/10.3390/ijms21134670. PMid:32630032.

41. Hoyois A, Ballarin A, Thomas J, Lheureux O, Preiser JC, Coppens E, et al. Nutrition evaluation and management of critically ill patients with COVID-19 during post–intensive care rehabilitation. JPEN J Parenter Enteral Nutr. 2021;45(6):1153-63. http://doi.org/10.1002/jpen.2101. PMid:33666263.

42. Cardon-Thomas DK, Riviere T, Tieges Z, Greig CA. Dietary protein in older adults: adequate daily intake but potential for improved distribution. Nutrients. 2017;9(3):184. http://doi.org/10.3390/nu9030184. PMid:28241469.

43. Wang PY, Li Y, Wang Q. Sarcopenia: an underlying treatment target during the COVID-19 pandemic. Nutrition. 2021;84:111104. http://doi.org/10.1016/j.nut.2020.111104. PMid:33421827.

44. Maiorino MI, Bellastella G, Longo M, Caruso P, Esposito K. Mediterranean diet and COVID-19: hypothesizing potential benefits in people with diabetes. Front Endocrinol. 2020;11:574315. http://doi.org/10.3389/fendo.2020.574315. PMid:33042027.

45. Papadopoulou SK, Detopoulou P, Voulgaridou G, Tsoumana D, Spanoudaki M, Sadikou F, et al. Mediterranean diet and sarcopenia features in apparently healthy adults over 65 years: a systematic review. Nutrients. 2023;15(5):1104. http://doi.org/10.3390/nu15051104. PMid:36904104.

46. Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clin Nutr. 2020;39(6):1631-8. http://doi.org/10.1016/j.clnu.2020.03.022. PMid:32305181.

47. Bauer J, Morley JE, Schols AMWJ, Ferrucci L, Cruz-Jentoft AJ, Dent E, et al. Sarcopenia: a time for action. An SCWD position paper. J Cachexia Sarcopenia Muscle. 2019;10(5):956-61. http://doi.org/10.1002/jcsm.12483. PMid:31523937.

48. Barrea L, Muscogiuri G, Frias-Toral E, Laudisio D, Pugliese G, Castellucci B, et al. Nutrition and immune system: from the Mediterranean diet to dietary supplementary through the

microbiota. Crit Rev Food Sci Nutr. 2021;61(18):3066-90. http://doi.org/10.1080/10408398.2020.1792826. PMid:32691606.

49. Venegas-Borsellino C, Sankararaman S, Roche K, Burns J, Landis RM. Impact of COVID-19 on the intestinal microbiome. Curr Nutr Rep. 2021;10(4):300-6. http://doi.org/10.1007/s13668-021-00375-z. PMid:34813042.

50. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30. http://doi.org/10.1210/jc.2011-0385. PMid:21646368.

51. Dissanayake HA, Silva NL, Sumanatilleke M, Silva SDN, Gamage KKK, Dematapitiya C, et al. Prognostic and therapeutic role of vitamin D in COVID-19: systematic review and meta-analysis. J Clin Endocrinol Metab. 2022;107(5):1484-502. http://doi.org/10.1210/clinem/dgab892. PMid:34894254.

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