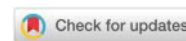


MUSCULOSKELETAL SYMPTOMS IN PATIENTS WITH POST COVID-19 SYNDROME AND OPPORTUNITIES FOR INCREASED FUNCTIONAL ACTIVITY

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Abstract: There is an increasing number of patients surviving SARS-CoV-2 infection who have no evidence of acute infection but who continue to have symptoms that persist and shape the post COVID-19 symptoms (PCS). Musculoskeletal symptoms (MSK), as part of the PCS, lead to reduced functional activity and cause prolonged suffering. The purpose of this review is to identify the main MSK symptoms in PCS and to review physical interventions that may have a beneficial effect in reducing MSK complaints and increasing functional activity in PCS. Materials and methods: A review of the literature was performed, including articles about MSK symptoms in patients with PCS and the possible physical interventions used in rehabilitation of these patients, with impact on symptoms, functional capacity, and functional activity. The scientific articles research took place in the bibliographic database of PubMed. The search results were found for: post-COVID-19 (PCS) syndrome, long COVID, post-acute sequelae of SARS-CoV-2 infection (PASC), chronic COVID syndrome (CCS), Musculoskeletal symptom, Pain post-COVID, physical function, Rehabilitation post-COVID, exercise, physical activity, functional capacity, traditional Chinese medicine. Results: The review found evidence of prolonged persistence of MSK symptoms as part of PCS syndrome. Fatigue, myalgia, back, waist and neck pain and arthralgia (pain in the peripheral joints) are the most reported symptoms. Data showing the need for rehabilitation and the positive effect of physical therapy and therapeutic exercises in patients with PCS to reduce pain and increase functional activity was found. Conclusion: Increasing physical activity in patients with PCS is likely to have a beneficial effect on general conditioning, physical function, and functional recovery, helping to overcome the effects of infection, reducing pain, and reducing emotional stress. Individually targeted physical interventions are recommended, including multimodal programs, exercises for overall muscle strengthening, increasing joint stability, cycling training. Individually targeted physical interventions are recommended, including multimodal programs, exercises for overall muscle strengthening, increasing joint stability, cycling training, electrical modalities - Transcutaneous electrical nerve stimulation (TENS) for pain symptoms. Rehabilitation should be applied after detailed functional assessment and shaped be carried out with the participation of a multidisciplinary rehabilitation team. The development of appropriate rehabilitation strategies will allow the achievement of optimal functional recovery and increased functional activity, satisfactory to the patient and will reduce the economic burden of prolonged reduced work capacity.

Keywords: Post-COVID-19 (PCS) syndrome, Musculoskeletal symptom, Pain post-COVID, Physical function, Rehabilitation post-COVID, Therapeutic exercise, TENS.

1. INTRODUCTION

The pandemic spread of coronavirus infection caused by coronavirus 2 (SARS-CoV-2) causing severe acute respiratory syndrome (Dong et al. (2020)) has posed new challenges to modern medicine and, at the same time, to healthcare systems worldwide. Although it mainly affects the respiratory system, COVID-19 is already considered a multisystem disease that is severe, often lethal (Barker-Davies et al. (2020)) and has a wide range of manifestations. Evidence has been gathered that coronavirus infection occurs not only with lung but also with cardiovascular, neurological, musculoskeletal, hepatic, renal, dermatological, psychosocial, and cognitive impairment (Barker-Davies et al. (2020); Shi et al. (2020); Herman et al. (2020); Zhang et al. (2020); Wang al. (2020)).

Like the post-acute viral syndromes described in other coronavirus epidemics, there have been increasing reports of persistent and prolonged effects after acute COVID-19. (Nalbandian et al. (2021)) The number of patients who have survived coronavirus infection and whose need for post-COVID care and recovery is increasing. The long-term effects of COVID-19 are not yet fully understood, but evidence of previous coronavirus infections indicates impaired pulmonary and physical function, reduced quality of life and emotional distress. Many patients who have survived COVID-19 need long-term medical care because of psychological, physical, and cognitive impairment. (Barker-Davies et al. (2020)).

The data collected and the accumulated clinical experience made it possible to describe a

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condition that can be identified as post-acute COVID-19 (PCS) syndrome, characterized by persistent symptoms and/or delayed or long-term complications after 4 weeks of onset of symptoms. Cardiovascular, neuropsychiatric, gastrointestinal, musculoskeletal, dermatological, or other general symptoms are observed (Nalbandian et al. (2021)). At present, the definition of a clinical case of PCS is not well defined (Augustin et al. (2021)). Various terms are used, such as "long COVID" (Mandal et al. (2021)), "chronic COVID syndrome" (Baig AM (2021)), "post-COVID syndrome" (Goërtz et al. (2021)), "post-acute COVID-19 syndrome" (Hirschtick Baig et al. (2021)).

The full clinical picture of PCS is complex and probably not fully described at this time. (Augustin et al. (2021)). It is likely that the ability of the virus to enter cells through the widely expressed ACE-2 receptor (Hoffmann et al. (2020)) leads to the possibility of many organs to undergo acute and chronic changes, which explains the heterogeneity of clinical symptoms. (Gavriatopoulou et al. (2020)).

A large number of patients in the recovery phase after SARS-CoV-2 have clinical symptoms months after the acute infection (Chopra et al. (2021)); Goërtz et al. (2021); Mandal et al. (2021)) and have not returned to the usual health condition. The ongoing assessment of PCS patients will become a key task in identifying and reducing the socio-economic and medical long-term effects of COVID-19. (Augustin et al. (2021)).

There are currently no uniform criteria for effective cause-and-effect treatment of PCS. Based on their clinical experience, Augustin et al. (2021) recommend further research and development of new therapeutic options for patients with PCS, which include individualized care by multidisciplinary teams and specific and general methods of physical rehabilitation.

2. MATERIALS AND METHODS

A review of publications, including articles related to MSK symptoms in patients with PCS and possible physical interventions used in the rehabilitation of these patients, which demonstrated effect on symptoms, functional capacity and functional activity was performed. The scientific articles search was conducted in the bibliographic database of PubMed and included articles published until February 14, 2022. The searched results were defining post-COVID-19 (PCS) syndrome, long COVID, post-acute sequelae of SARS-CoV-2 infection (PASC), chronic COVID syndrome (CCS), Musculoskeletal symptom, Pain post-COVID, Physical function, Rehabilitation post-COVID, exercise, Physical activity, Functional capacity, traditional Chinese medicine. The review examines published, available randomized studies, recommendations, prospective controlled clinical trials, reports, guidelines, letters to the editor in English, meeting the set search criteria.

3. RESULTS

The review of the available publications found evidence of prolonged persistence of musculoskeletal symptoms as part of the post-COVID-19 (PCS) syndrome. Fatigue, myalgia, back, waist and neck pain, and arthralgia (pain in the peripheral joints) are most reported. Data showing need for rehabilitation and the positive effect of the physical therapy and the therapeutic exercises in PCS in reducing pain and increasing functional activity were found.

4. DISCUSSIONS

Prolonged health effects can occur even after very mild COVID-19 treated in an outpatient setting. Augustine et al. (2021) report that in about 81% of all infected patients, the disease is mild (WHO 2020), and PCS can be expected to affect more individuals than originally thought and that these effects will pose medical, social, and economic challenges. Males are associated with a lower PCS risk. (Augustin et al. (2021)). In a large prospective study, Augustin et al. (2021) with 958 convalescent patients after mild SARS-CoV-2 infection in 12.8% - 27.8% long-term health effects and at least one symptom (anosmia, ageusia, fatigue or shortness of breath) at fourth and seventh month after the illness were reported. Lower SARS-CoV-2 IgG titer at the beginning of the follow-up period is associated with a higher incidence of PCS. Low IgG levels six weeks after the onset of symptoms may lead to an insufficient humoral immune response, which is likely to be the cause of long-term PCS in these patients.

Severe COVID-19 infection causes catabolic muscle loss, difficulty eating and weakness, which may be the probable cause of bad treatment outcomes. (Hosey & Needham (2020)). Many studies

after acute COVID-19, which include assessments of health-related measurements of quality of life and functional capacity, report significant functional deficits, even 6 months after the infection. (Carfi et al. (2020); Chopra et al. (2020)) It is assumed that early rehabilitation programs are both safe and effective (Nalbandian et al. (2021)).

The exact musculoskeletal consequences after COVID-19 have not yet been described, but it has been found in patients admitted to the intensive care units during previous epidemic outbreaks that these patients needed rehabilitation due to MSK complications (Chan et al. (2003); Barker-Davies et al. (2020)). In a systematic review, Appleton et al. (2015) reported that patients undergoing intensive care and those undergoing mechanical ventilation are prone to develop muscle weakness and physical impairment (Appleton et al. (2015)). Muscle changes that involve atrophy and loss of muscle mass begin to develop as early as the first week (Barker-Davies et al. (2020)). These changes should be taken into account during the recovery period and in patients with PCS, because the presence of general muscle weakness and deconditioning can slow down and complicate the recovery process. Lower levels of physical function are also associated with deteriorating quality of life in the recovery period after acute infection of patients (Hui et al. (2005); Rooney et al. (2020)). Musculoskeletal symptoms of fatigue, myalgia and arthralgias are common in COVID-19. (Vaishya et al. (2021)). Accurate assessment of functional capabilities is needed, and it will allow the gradual inclusion of physiotherapy methods that are most effective in terms of functional recovery of patients, without inadequately burdening the cardiovascular and the respiratory systems.

The outcomes of studies show that patients with PCS have at least one symptom (Carfi et al. (2020); Huang et al. (2021)) Carfi et al. surveyed 143 patients for an average of 60.3 days after the onset of the first symptom. Only 12.6% were completely asymptomatic after COVID-19, while 32% had 1 or 2 symptoms and 55% had 3 or more: fatigue (53.1%), shortness of breath (43.4%), joint pain (27.3%) and chest pain (21.7%). 87.4% reported persistence of at least 1 symptom. None of the patients had fever or symptoms of acute illness. Deteriorated quality of life is observed in 44.1% of patients (Carfi et al. (2020); Huang et al. (2021)).

Bakilan et al. (2021) in a retrospective study of 280 patients with PCS, divided into two groups: 1 - patients whose MSK symptoms began or worsened by COVID-19 and patients with no MSK changes related to COVID-19. They reported that 88.2% had at least one or more symptoms, regardless of gender, 85.7% had at least one or more MSK symptoms that had started or worsened with COVID-19, while MSK problems in 14.3 % of the patients have not changed since COVID-19. The most common symptoms are fatigue (71.8%), back spine pain (70.7%) and myalgia (60.7%). The most common area of spine pain is the back (30.4%). The incidence of dyspnea is 30%, cough 18.5% and chest pain 10.7%. (Bakilan et al. (2021))

Karaarslan et al. (2021) in a prospective study of 300 patients found that about three-quarters of the participants had one or more symptoms, and 56.3% of them some MSK symptom at 1st month. The most common MSK symptom is fatigue (44.3%), followed by back pain (22.7%), arthralgia (22.0%), myalgia (21.0%), low back pain (16.3%). % and neck pain (10.3%) at 1st month. The study proved that the increased BMI is associated with a higher likelihood of persistence of fatigue, myalgia, and arthralgia at 1st month, but there is no relationship discovered associated with age/sex/length of hospital stay and the persistence of these symptoms. (Karaarslan et al. (2021))

According to Rooney et al. (2020) appropriate type and dosage of exercises necessary to achieve beneficial effects on the post-infectious condition should be selected. Exercises need to be modified at different stages of recovery to optimize recovery of function. In addition, attention should be paid to the way the exercises are performed to ensure safety and effectiveness of the intervention (Rooney et al. (2020)).

Zheng et al. (2015) in a study observed a decrease in the secretion of tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) in response to non-antigenic stimulation in a group that regularly engages with physical activity compared to the control group. Probably moderate activity supports a healthy immune response to infection and suppresses autoimmune activity in the absence of infection, while reduced physical activity impairs the immune response. (Barker-Davies et al. (2020)). Decreased physical activity leads to increased insulin resistance, which may be the cause of impaired immune response against microbial agents, including activation of macrophages and proinflammatory cytokines. (Luzy et al. (2020)). Exercise may play an important role in influencing the immune response, which may also be important. (Barker-Davies et al. (2020)).

At this stage, a lot of data has been collected and reported from studies and meta-analyzes that exercise is effective in terms of health and causes both short-, medium-, and long-term positive effects associated with preventing and delaying the development of metabolic, pulmonary, cardiovascular

vascular, neurocognitive, inflammatory, rheumatic, and musculoskeletal diseases (Jimeno-Almazán et al. (2021); Metsios, Moe & Kitas (2020); Posadzki et al. (2020); Rueggsegger & Booth (2018)). Decreased physical activity is thought to be associated with a higher risk of severe post-COVID 19 symptoms (Jimeno-Almazán et al. (2021); Salliset al. (2021)) and it is likely that exercise applied could be beneficial in patients with PCS. Symptom-appropriate physical activity and exercise are recommended for the rehabilitation of these patients (Jimeno-Almazán et al. (2021)).

Individually targeted exercise is highly recommended as a non-pharmacological treatment for rheumatic and MSK diseases in which there is chronic pain, muscle weakness, physical limitations, fatigue, and low tolerance to exercise. (Jimeno-Almazán et al. (2021); Metsios, Moe & Kitas (2020); Rausch Osthoff et al. (2018); Hilberdink et al. (2020)). Strength training and multicomponent exercise programs are recommended as safe and effective in reducing weakness and restoring functional capacity. (Jimeno-Almazán et al. (2021); Courel-Ibáñez et al. (2021); Cadore et al. (2021)). In addition, regular exercise can affect depression and anxiety, reduce psychological stress, and modulate pain perception, thus improving the quality of life. (Chen et al. (2020))

A strategy that includes overall muscle strengthening, including cycling, could probably be effective. In adult patients with limited daily activity, Occupational therapy is recommended with the aim to increase their autonomy. (Asly & Hazim (2020)) For this purpose, it is recommended to test the patient's assessment of daily living activities (ADL), including Basic Daily Living Activities (BADL) and Instrumental Daily Living Activities (IADL). (Demeco et al. (2020))

Nalbandian et al. (2021) in a review reported that joint pain was the third most common consequence (27.3%) after fatigue (53.1%) and dyspnea (43.4%). Onset and persistence of chronic pain after COVID-19 is becoming an increasingly pressing issue for pain rehabilitation and control. (Kemp, Corner & Colvin, (2020); Clauw et al. (2020); Angotti et al. (2022)) Bakılan et al. (2021) reported that back pain is the most common symptom of PMR outpatient care, with the most common musculoskeletal symptoms being fatigue, back pain, and myalgia. They found that back pain, low lymphocyte counts and higher levels of D-dimer, as well as CAT findings in the lung in acute COVID-19, prolonged hospitalization, and chronic disease were likely to contribute to PCS and MSK symptoms. (Bakılan et al. (2021))

To reduce pain, Wang et al. (2020) propose the application of transcutaneous electrical nerve stimulation (TENS). TENS is a physical modality that works in the low frequency range and is characterized by parameters capable of stimulating the sensory and peripheral nerves. Applied with the purpose to reduce pain, TENS stimulates A fiber to reduce pain, the action of which is explained by the gate control theory. (Tashani & Johnson (2009)) Studies show that TENS can successfully reduce acute and chronic pain. (Tang et al. (2017); Wang et al. (2020)) in order to optimize the analgesic effect, it is recommended that TENS parameters are set individually. (Tang et al. (2017)) Concurrent use of TENS and therapeutic exercises (can also be performed at home) is recommended, such as stretching exercises in the affected area, strengthening exercises to increase stability and to facilitate strengthening peripheral weak muscles to improve stability. Strengthened muscles and improved stability can help reduce the pain of instability. (Steilen et al. (2014)). In chronic pain for more than 6 months, exercises to facilitate weak muscles in combination with drug therapy are recommended (Wang et al. (2020))

Application of traditional Chinese medicine (TCM) methods is likely to promote functional recovery after the acute phase of COVID-19, but there is still no evidence that TCM can be an effective option for restoring body functions. (Sun et al. (2020)) Feng et al. (2020) suggest that Qigong is likely to be potentially effective in the prevention, treatment, and rehabilitation of COVID-19. They suggest several mechanisms of action to reduce stress, regulate emotions, strengthen respiratory muscles, reduce inflammation, and strengthen immune function. (Feng et al. (2020))

Active participation and assistance of patient are important for the success in the process of functional recovery and rehabilitation. Psycho-emotional instability, anxiety, or refusal to cooperate or incomplete cooperation could negatively affect the results. The presence of cognitive dysfunction, fatigue, or depression in patients with PCS may affect the outcome and effectiveness of rehabilitation. (Rooney et al. (2020))

Unexpected complications from concomitant diseases may occur during rehabilitation. This may temporarily stop or delay rehabilitation, but rehabilitation should begin as soon as possible after the complication has been resolved. At the same time, rehabilitation activities need to be adequately dosed so that they do not lead to complications.

Physical and rehabilitation medicine (PRM) is focused not only on the functional recovery of patients with chronic disabling conditions, but also in patients during the convalescent period and with combined pathologies, with the aim to reduce the duration of treatment. (Grabowski et al. (2020)) New questions arise that require creation of new patterns of behavior, such as how many patients with COVID-19 need

rehabilitation, how effective and safe rehabilitation strategies can be, what are the possible problems and complications, which physical modalities will be effective for optimal functional recovery.

In moderate and severe infections during the convalescence period, residual changes are possible, such as fibrotic changes, which in the future may lead to respiratory disorders or problems with reduced physical tolerance (Huang et al. (2020); Choon-Huat Koh, G., & Hoenig, H. (2020)) in combination with persistent MSK symptoms and reduced functional activity. The rehabilitation of PCS requires the formation of a multidisciplinary rehabilitation team, with the participation of various specialists. The activities of the rehabilitation team should be coordinated by a specialist in Physical and Rehabilitation Medicine depending on the needs of the individual patient in order to improve the effectiveness of rehabilitation and to provide comprehensive medical care. In preparing and implementing rehabilitation programs it is necessary to follow the basic principles of PRM for individual approach to each patient, gradual increase in load, comprehensiveness of different muscle groups, and in rehabilitation it is necessary to take into account the general clinical condition and psycho-emotional patient tone. New development opportunities are emerging for PRM, such as telemedicine, and in particular telerehabilitation, as an effective alternative for patients with COVID-19, as well as patients with chronic diseases. (Papathanasiou et al. (2022))

5. CONCLUSIONS

Increasing physical activity in patients with PCS is likely to have a beneficial effect on general condition, physical function, and functional recovery, helping to overcome the effects of infection, reducing pain, and reducing emotional stress. Individually targeted physical interventions are recommended, including multimodal programs, exercises for overall muscle strengthening, increasing joint stability, cycling training, electrical modalities (TENS) for pain symptoms. Rehabilitation should be applied after detailed functional assessment and should be carried out with the participation of a multidisciplinary rehabilitation team. At this stage, the study of musculoskeletal symptoms in PCS continues. A better understanding of the syndrome itself, the pathophysiological mechanisms of its occurrence, duration and severity of complaints will help to develop appropriate pharmacological treatment and rehabilitation strategies that will achieve optimal functional recovery and increased functional activity, satisfying the patient and to reduce the economic burden of reduced working capacity.

Conflict of interests

The author declares no conflict of interest.

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