



# Physical Medicine and Rehabilitation Management in Patients with Long COVID-19 and Thymoma-associated Myasthenia Gravis: A Case Report

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## Abstract

**Background:** Myasthenia gravis is an autoimmune disease that causes muscle weakness and fatigue due to antibodies attacking the acetylcholine receptor. In patients with MG, fatigue can be worsened by concurrent long COVID, leading to further deterioration of cardiorespiratory function.

**Case:** A 44-year-old woman with long COVID syndrome and thymoma-associated myasthenia was given an exercise program that aimed to overcome fatigue so that the patient could carry out her role as a housewife, and to prepare for thymectomy surgery. Before exercise, patients were educated to take pyridostigmine 1 hour earlier. During exercise, the patient was monitored to prevent excessive fatigue. At the end of the training session, the patient was asked to observe for signs of exacerbation until the next training session.

**Discussion:** Pulmonary rehabilitation (PR) can be beneficial for patients with thymoma-associated MG and long COVID-19, but it requires special strategies. PR typically starts with light weights and gradually increases in intensity. It has been shown to improve fatigue and cardiorespiratory endurance, as indicated by a successful 6-minute walk test after 4 weeks of training intervention.

**Conclusion:** Pulmonary rehabilitation plays an important role in increasing cardiorespiratory endurance and functional capacity for surgery preparation. The provision of pulmonary rehabilitation programs must be tailor-made according to the patient's functional ability and underlying disease to achieve optimal goals.

**Keywords:** long COVID-19, myasthenia gravis, thymoma

## INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder in which the body's immune system attacks the acetylcholine

receptor (AChR), a protein that helps nerves send signals to muscles. This can decrease muscular endurance and respiratory complications. A thymoma is a

tumor of the thymus gland that is associated with MG. About 10-20% of people with MG have thymoma, and about 30% of people with thymoma have a secondary MG. The first line of treatment for thymoma has been recommended to be thymectomy.<sup>1,2</sup>

Presently, there is no evidence to support a connection between COVID-19 infection and the onset of MG. Due to several circumstances, including decreased baseline respiratory efficiency and the immunocompromised state brought on by immunosuppressive therapy, patients with MG are more likely to contract severe COVID-19. The use of immunosuppressive corticosteroids is associated with an increased risk of infection, up to 50%.<sup>3</sup>

The subacute and long-term consequences of COVID-19, which can influence numerous organ systems, are being studied by clinical evidence and science. According to early reports, SARS-CoV-2 infection may still cause symptoms like fatigue, chest pain, dyspnea, cognitive problems, and a deterioration in quality of life.<sup>4</sup>

Pulmonary rehabilitation can help improve physical function, endurance, performance, and participation in work and social activities for people with lung diseases.<sup>5</sup> In this case report, we will describe the role of pulmonary rehabilitation in patients with long COVID syndrome and thymoma-associated myasthenia gravis and preparation for thymectomy surgery.

## CASE

A 44-year-old female patient was consulted to the rehabilitation department in preparation for surgery with dyspnea on effort caused by long COVID-19 syndrome and thymoma-associated MG in early 2022. She complained of shortness of breath, especially when speaking, coughing, doing household activities, and ambulating inside the house.

The patient was diagnosed with a thymoma in 2012 and has not been operated on. In 2015, she was also diagnosed with MG and received pyridostigmine 240 mg/day, methylprednisolone, and azathioprine. In 2017, the patient experienced shortness of breath again and was treated at the hospital with plasmapheresis 5 times, and the pyridostigmine dose was increased. Afterward, the patient experienced no symptoms of shortness of breath or weakness.

In 2021, the patient was hospitalized once more due to complaints of shortness of breath, weakness, especially the eyelids that were difficult to open and close in the afternoon, coughing with phlegm, and painful swallowing. The results of the PCR COVID-19 test were positive. She was treated in the intensive care unit and supplemented with oxygen using a high-flow nasal cannula at 21 lpm and FiO<sub>2</sub> of 70%. At that time the patient was diagnosed with moderate acute respiratory distress syndrome due to COVID-19 and myasthenia gravis.

After treatment, the patient was still on oxygen supplementation and succeeded in not using oxygen 9 months later. In 2022, the patient was exposed to COVID once again, hospitalized, and still used oxygen only when needed after returning home.

In the Department of Medical Rehabilitation, the patient received supplemental oxygen through a nasal cannula after returning from the bathroom, as she had up to 86% oxygen desaturation. She underwent pulmonary rehabilitation in the form of aerobic exercise using an ergo cycle accompanied by oxygen supplementation and breathing exercises twice a week, for a total of 6 times.

After the patient had carried out 1 series of pulmonary rehabilitation, she came for an evaluation, and currently, complaints of fatigue have been much reduced. However, the shortness of breath still existed when she was doing daily activities. She was able to carry out daily activities independently, walking for about 10-15 minutes, and was less likely to use oxygen supplementation, but for household activities, she still often felt tired.

On physical examination, vital signs were within normal limits with oxygen saturation of 99% in room air, the BORG scale was 6-0-0, the BMI was 27.05 kg/m<sup>2</sup>, and the fatigue severity scale decreased from 62 to 51. Chest expansion enlarged from previous 2-3-4 cm to 3-3.5-4 cm. On auscultation, bilateral pulmonary vesicular breath sounds were

obtained while rhonchi, wheezing, and phlegm were absent.

In the single breath count test, 17 results were achieved whereas previously it was only 7. Sit-to-stand test for 30 seconds: the patient could do it 9 times, which was still the same as the previous examination. The 6-minute walk test result was 255 meters with a predicted VO<sub>2</sub> max of 12.4 ml/kg/min and converted to METs of 3.54 METs.

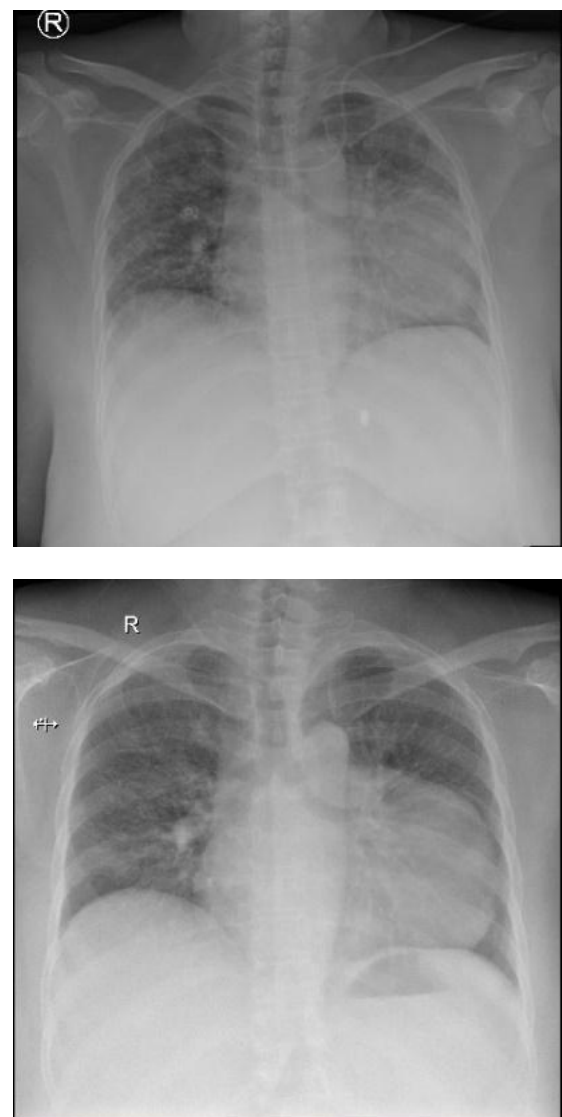


Figure 1. Chest radiograph 2021 (top) and 2022 (bottom)

On chest x-ray (CXR) examination (Figure 1), pneumonia was found in both

lungs, in conjunction with left mediastinal mass, aortic elongation and calcification. The CT scan of the thorax revealed diffuse ground glass opacity and thickening of the interlobular septa in almost all segments of both lungs with suspected pneumonia, a left anterior mediastinal mass attached to the pleura and pericardium, and a mass in the supraclavicular to the superior mediastinum, relatively the same size, multiple.

## DISCUSSION

A neuromuscular junction autoimmune illness called myasthenia gravis is clinically characterized by the weakening and fatigue of several skeletal muscles. Antibodies that directly affect the neuromuscular junction are the clinical hallmark of striated muscle weakness. Muscular weakness in MG can influence the ocular, limb, respiratory, and bulbar muscles; it can change over time and is frequently brought on by exertion.<sup>6,7</sup>

Due to the risk of overloading weakened muscles, physicians who treat patients with neuromuscular disorders have typically been reluctant to actively encourage physical activity. Modern immunosuppressive, symptomatic, and supportive treatments have advanced to the point where most well-controlled MG patients now have a positive outlook, a normal life expectancy, and minimal impact on daily activities.<sup>6,7</sup>

The evaluation of physical activity in MG presents certain difficulties in measuring fatigue objectively. Exercise

triggers an immunological response that results in an increase in T regulatory cells, a decrease in immunoglobulin secretion, and a change in the Th1/Th2 balance that favors decreasing the production of Th1 cells.<sup>6</sup>

Exercise can be challenging for people with MG due to proximal muscle weakness, fatigue, and respiratory muscle dysfunction.<sup>6</sup> The prevalence of fatigue in MG is similar to that of other neuromuscular disorders, with rates between 61–74% in facioscapulohumeral muscular dystrophy (FSHD), myotonic dystrophy, and hereditary motor and sensory neuropathy type 1.<sup>3</sup> Fatigue in MG patients can be caused by several factors, including female gender, the presence of both anticholinergic receptor and muscle-specific receptor tyrosine kinase (MuSK) antibodies, and higher depression rates.<sup>7</sup>

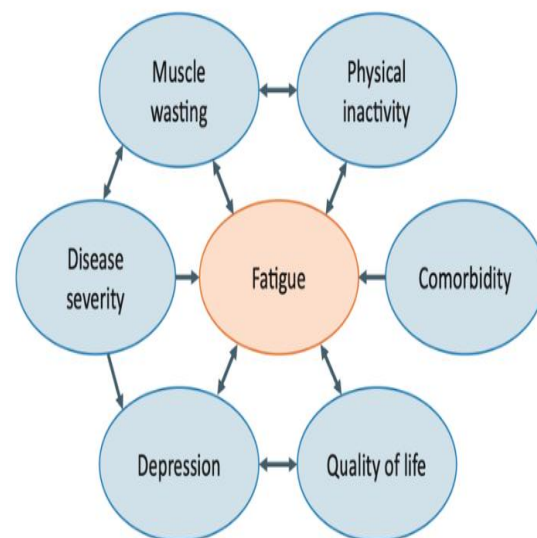


Figure 2. Model illustrating how fatigue is multifaceted<sup>7</sup>

It has been theorized, based on some studies, that muscular damage causes fatigue (Figure 2) via a central nervous

system-driven process to momentarily down-regulate physical activities and keep muscles from injury. In patients with neuromuscular diseases, chronically low levels of physical activity likely have a deleterious impact on muscle mass and

strength, creating a vicious cycle. Obesity can result from a lack of physical activity. A significant proportion of MG patients are overweight (BMI  $\geq 25$ ) as a result of their combination of prolonged steroid treatment and inactivity.<sup>7</sup>

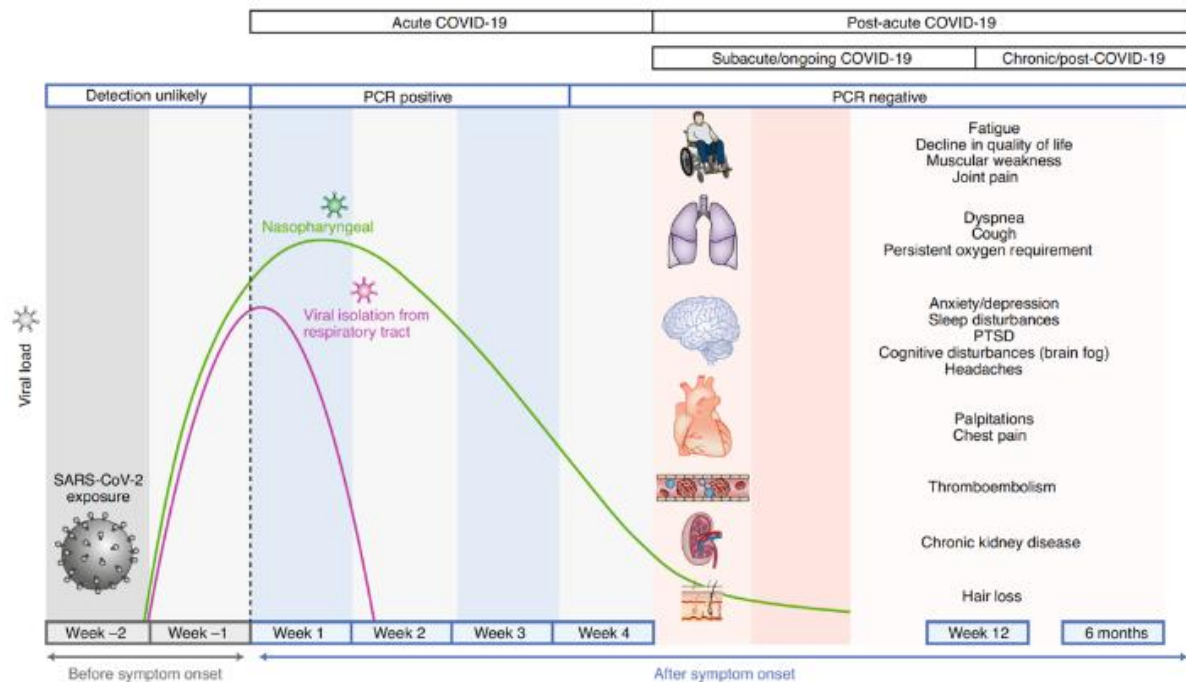


Figure 3. Timeline of post-acute COVID-19<sup>4</sup>

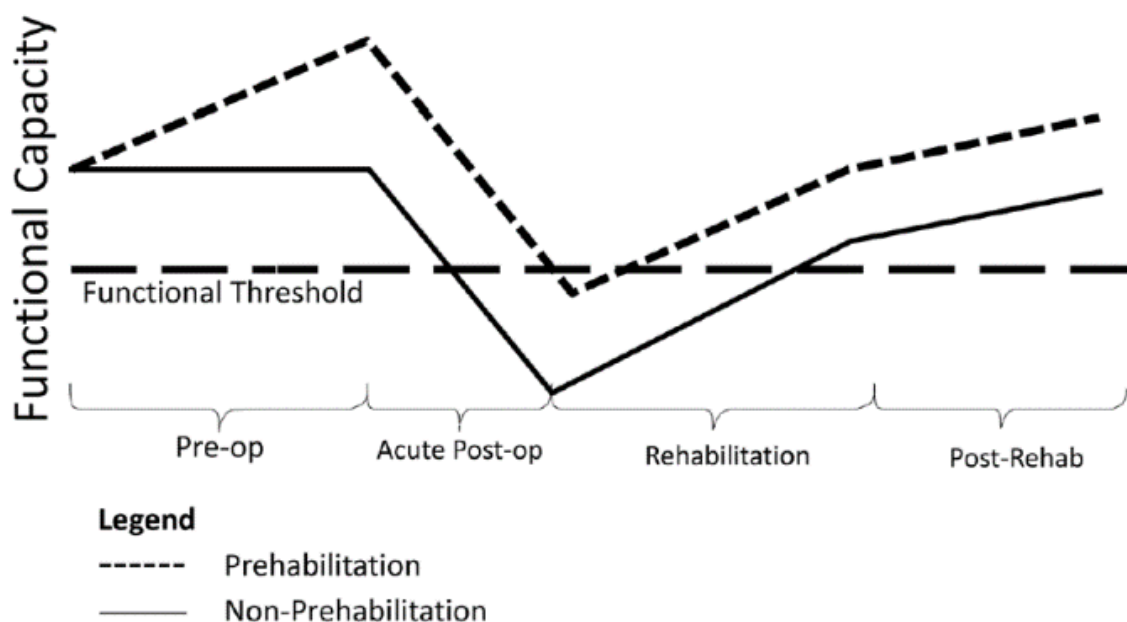


Figure 4. Conceptual model of generalized functional ability progression in patients receiving prehabilitation vs. simply rehabilitation prescriptions<sup>8</sup>

Post-acute COVID-19 is a condition that can occur after a SARS-CoV-2 infection. It is characterized by persistent symptoms and/or delayed or long-term complications that develop more than 4 weeks after the onset of symptoms.<sup>4</sup>

Figure 3 illustrates the timeline of post-acute COVID-19 into two categories: subacute or ongoing symptomatic COVID-19, which is characterized by symptoms and abnormalities that are present from 4 to 12 weeks after the onset of acute COVID-19, and chronic or post-COVID-19 syndrome, which is characterized by symptoms and abnormalities that persist or are present more than 12 weeks after the onset of acute COVID-19, and are not caused by other conditions.<sup>4</sup> This is what caused the patient's fatigue to worsen, especially post-COVID-19.

Numerous physical conditions can be treated with surgery, but this major stressor frequently has negative impacts on a patient's ability to carry out daily activities and decreases the quality of life. Prehabilitation is a method of preparing surgery candidates using multiple techniques (Figure 4) intended to enhance their physical, physiological, metabolic, and psychosocial reserves.<sup>8</sup>

Prehabilitation is the process of improving physical and mental health to protect against the potentially harmful effects of surgery. It involves preoperative physical and psychological conditioning to build up bodily and mental fitness and prevent the anticipated functional and well-being declines associated with surgery.<sup>8</sup>

Patients receive treatment on an outpatient basis. Pulmonary rehabilitation is provided in the form of breathing control exercises, chest expansion exercises, aerobic exercises, and strengthening exercises. Before training, patients were given education to consume pyridostigmine. The peak effect of pyridostigmine is about 30 to 60 minutes after consumption. During exercise, the patient is still asked to do breathing control so that the lungs continue to work efficiently.

Exercises are given slightly differently from the patient in general. Patients with MG and long COVID syndrome tend to get tired quickly, so the dose of exercise, especially resistance training, starts with light weights and then progressively increases. After the exercise, the patient was asked to evaluate whether there were symptoms of exacerbation of MG.

Rehabilitation plays an important role in the management of post-COVID-19 syndrome. Studies pointed out that endurance, strength, inspiratory muscle training, expectorant training, and diaphragm training exhibited improvement from baseline.<sup>9-11</sup> Rehabilitation programs should be personalized, safe, and supportive to sustain function without symptom exacerbation.<sup>12</sup>

Other studies concluded that cardiopulmonary rehabilitation consisted of aerobic exercise, muscle strengthening, and respiratory exercise 3 times per week over 8 weeks indicated improvement.<sup>13</sup> However, early rehabilitation is vital for the long-term recovery and functional

improvements of post-COVID-19 syndrome patients.<sup>14,15</sup>

## CONCLUSION

The pulmonary rehabilitation program is effective in increasing cardiorespiratory endurance, and it plays an important role in preparing patients for surgery to increase their functional and mental capacity when dealing with physiological stressors from surgery and anesthesia. After the rehabilitation program, the patient shows improvement in shortness of breath, fatigue severity scale, chest expansion, single breath count test, and the 6-minute walking test. Pulmonary rehabilitation programs must be tailor-made according to the patient's functional ability and underlying disease to achieve optimal goals.

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