



Graded exercise therapy for individuals with long COVID syndrome and postexertional malaise: Pro et Contra | 1

The infection with severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) can lead to a new disease called long-COVID-19 or post-acute COVID-19 syndrome (PACS). This syndrome can occur in various populations, including children, young adults, and those who had only mild COVID-19. Long COVID/PACS represents a heterogeneous nosological entity, despite similar or overlapping symptoms between patients, and clear diagnostic criteria are yet to be established. The most frequent symptoms of post-COVID syndrome include fatigue, muscle weakness, dyspnea, cough, headache, cardiac arrhythmias, palpitations, cognitive impairment, and anxiety/depression. A significant number of individuals with PACS exhibit neurological sequelae that include autonomic imbalance and exercise intolerance. This autonomic imbalance significantly overlaps with dysautonomia syndrome observed in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). In their recent articles, several authors have discussed the clinical management of autonomic dysfunction and graded exercise therapy for individuals diagnosed with long COVID/PACS syndrome.

Some authors have suggested that neurorehabilitation and multimodal therapy can be delivered in outpatient and inpatient settings. Occupational therapy was recommended as a cornerstone of rehabilitation in individuals with post-COVID syndrome. Diem L. and coworkers suggested that patients with PACS should use therapies proven successful in patients with multiple sclerosis, such as energy management education. They also recommended pacing, which establishes the optimal and individual balance between rest and activation periods (physical, cognitive, and emotional). This energy conservation strategy is known as the “Principle of Three Ps”, namely, prioritization, planning, and pause in everyday activities. Diem L. et al. The Role of Neurorehabilitation in Post-COVID-19 Syndrome. *Clin. Transl. Neurosci.* 2023, 7, 13. <https://doi.org/10.3390/ctn7020013>

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Other authors have recommended that physical activity should be adapted with individual limitations to avoid severe post-exertional malaise. Fedorowski et al. recommended graded exercise therapy in patients with post-exertional malaise based on the PACE trial that reported positive outcomes of graded exercise therapy and cognitive behavioral therapy in patients with ME/CFS. Fedorowski et al. Cardiovascular autonomic dysfunction in post-COVID-19 syndrome: a major health-care burden. *Nat. Rev. Cardiol*

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However, a group of authors from the Netherlands, Austria, Germany, and the United States expressed disagreement with the recommendations for graded exercise therapy for individuals diagnosed with long COVID syndrome who suffer from postexertional malaise. Van Rhijn-Brouwer et al. pointed out that research that used modern, more accurate diagnostic criteria for postexertional malaise showed that exercise-based therapies frequently result in detrimental health outcomes for patients with ME/CFS.

Van Rhijn-Brouwer et al. stated that up to 85% of patients with long COVID syndrome can have a combination of postexertional malaise and cardiovascular autonomic dysfunction. They emphasized that patients with long COVID/PACS syndrome should be classified according to the presence of postexertional malaise, and that graded exercise therapy should be avoided in individuals with long COVID and postexertional malaise. To support their views, the authors cited a previous cross-sectional study that demonstrated that 75% of 477 participants diagnosed with PACS reported a worsening of symptoms and functional



capacity after exercise therapy.

Van Rhijn-Brouwer et al. added that the recommendations in the article by Fedorowski et al. can be followed only in individuals with long COVID without postexertional malaise, and with ongoing surveillance for the emergence of postexertional malaise. They concluded that individuals with long COVID and postexertional malaise should be supported in maintaining their daily activities within their available funds of energy. These patients should be managed by employing other nonpharmacological and pharmacological interventions outlined in the article by Fedorowski et al.

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Journal Reference

van Rhijn-Brouwer, F.C.CC., Hellemons, M., Stingl, M. et al. Graded exercise therapy should not be recommended for patients with post-exertional malaise. Nat Rev Cardiol (2024). (Open Access) <https://doi.org/10.1038/s41569-024-00992-5>