Exercise Therapy for Post–COVID-19 Condition—Does No Harm

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International guidelines from public health organizations, including the World Health Organization, caution against graded exercise for treating patients with postexertional symptom exacerbation (PESE), a commonly reported feature of post–COVID-19 condition (PCC). These recommendations are provided despite the well-documented deleterious effects of physical inactivity and its close association with secondary health conditions and deterioration in quality of life. Subsequently, there has been confusion and reluctance among health care practitioners to prescribe exercise-based rehabilitation to individuals with PCC to avoid the debilitating effects of postexertional malaise, fatigue, or PESE. Consequently, the effects of exercise-based rehabilitation for individuals with persistent PESE remain poorly understood. Studies have shown that among individuals with PCC, up to 48% of female individuals and 41% of male individuals experience postexertional malaise, and 29% of female individuals and 28% of male individuals experience orthostatic intolerance. The article by Tryfonos and colleagues is, therefore, timely and necessary because it addresses an important topic in the debate surrounding patient acceptability and the therapeutic effects of different exercise modalities in the treatment of patients with PCC and their acute risks of developing PESE.

Tryfonos et al recruited 31 nonhospitalized, community-based participants with a mean (SD) symptom duration of 21.6 (9.2) months following COVID-19 illness (with 31 age-matched and sex-matched healthy controls for comparison). This previously healthy and working-age population represents an important section of society: 78% of the PCC group were employed full-time before SARS-CoV-2 infection. Subsequently, 74% had to take sick leave lasting longer than 12 months. PCC, therefore, has a substantial economic impact on nonhospitalized, working-aged individuals, a challenge that is magnified if job roles are cognitively and/or physically demanding. The careful introduction and future management of exercise therapy in the treatment of individuals with postviral conditions has been previously proposed following a comprehensive needs analysis to mitigate PESE. This can be achieved by individually tailoring exercise prescription and/or management and incorporating both resistance exercise and cardiorespiratory fitness, in an approach termed symptom-guided exercise rehabilitation. Testing this theory, Tryfonos and colleagues monitored the acute effects of 3 different types of exercise stimulus in those with PESE, compared with healthy controls, aware that patients with PCC spent 43% less time in moderate-to-vigorous physical activity compared with controls (approximately 26.5 minutes per day). The 3 exercise modalities were (1) high-intensity interval training (HIIT), (2) moderate-intensity continuous training (MICT), and strength-based training (ST) performed in a randomized, crossover design with 2 to 4 weeks of washout between sessions. The primary outcome measure was the difference in fatigue level (from baseline to 48 hours after exercise) between groups. The authors chose this time, citing that those with phenotypically similar myalgic encephalomyelitis–chronic fatigue syndrome commonly report PESE between 24 and 72 hours after exertion. Reassuringly, there were no between-group differences in fatigue 48 hours after any exercise modality (HIIT, MICT, or ST). However, subtle differences in self-reported symptoms were observed following each exercise condition, with patients with PCC reporting higher levels of concentration impairment following MICT and greater increases in muscle soreness after ST (commensurate with delayed onset of muscle soreness, which is expected after completing unfamiliar loaded resistance exercise).

Compared with healthy controls, the PCC group had higher overall self-reported symptom scores at all time points (before exercise, immediately after exercise, and at 48 hours follow-up).
alongside substantial physiological characteristics; indeed, a particular strength of this study\textsuperscript{2} is the range of physiological assessments undertaken. The PCC group demonstrated underlying dysfunction in multiple organ systems that may contribute to activity limitations, including muscular impairment (ie, higher incidence of myogenic-derived myopathies observed alongside decreased isometric muscle strength), indices of orthostatic intolerance, lower peak and submaximal aerobic capacity (ie, maximal oxygen consumption at peak and ventilatory threshold), lower heart rate variability (recorded during deep breathing), higher resting heart rate, and increased arterial stiffness. Tryfonos et al\textsuperscript{2} proposed mechanisms, including physical inactivity, peripheral tissue damage, and/or neurophysiological changes, for these physiological limitations, echoing findings from other research groups.\textsuperscript{5} These clinical manifestations present a complex rehabilitation challenge, requiring modulation of activity duration and/or intensity, with concurrent pacing, to avoid PESE or fatigue.

Debunking the controversies surrounding graded exercise therapy, reinforcing the importance of physical activity, and integrating resistance exercise and cardiorespiratory fitness into the rehabilitation programs for individuals with postviral conditions formed the basis of a recent clinical commentary.\textsuperscript{4} The article by Tryfonos and colleagues\textsuperscript{2} reinforces some of those key messages with quantifiable data. The ability of individuals with PCC to tolerate various exercise activities, particularly hard-intensity activities (scoring $\geq$16 on the 6-20 rate of perceived exertion Borg scale) without major escalation of symptoms, fatigue, or exercise capacity is important for advancing rehabilitation provision and practice in those with PESE. From an exercise prescription perspective, continued engagement with either endurance-based exercise session (HIIT and MICT) provides the opportunity to improve cardiorespiratory fitness. Importantly, both exercise types meet patient acceptability, do not exacerbate symptoms of fatigue, and provide options to patients with PCC regarding individual training preferences (vigorous-intensity 10-minute HIIT session vs moderate-intensity, 30-minute MICT session).

This study\textsuperscript{2} demonstrates the acute response to different exercise modalities, which was largely comparable between groups with no profound symptom exacerbation. These findings are extremely important as a proof of concept but require a longitudinal trial to determine whether these exercise modalities remain feasible to deliver in a community setting, are acceptable on behalf of the patient, and elicit favorable longer-term outcomes. However, it is important to note that this study involved individuals with no known comorbidities. Prescreening and appropriate adjustments to exercise volume and/or intensity may be warranted when accommodating secondary health conditions and to a wider population. We recognize that greater rehabilitation support, education, and creativity may be warranted to attain favorable long-term changes in physical function and counteract the effects of prolonged muscle deconditioning in individuals with complex rehabilitation needs. If these exercise sessions can be carefully incorporated into a longitudinal exercise protocol, they may have far-reaching positive health consequences for individuals with PCC, including improvements in cardiorespiratory, musculoskeletal, and mental health, with subsequently reduced work absenteeism. Further complementing this study's findings is a recent prospective cohort study\textsuperscript{6} that reported increased physical activity levels alongside reductions in PESE episodes (from 3.4 to 1.1 per week) following a supervised progressively structured 6-week pacing protocol within a post–COVID-19 rehabilitation service.

Given the consequences of physical inactivity on muscle mass, muscle strength, and cardiorespiratory fitness, strategies that encourage participation in exercise rehabilitation programs are vital if we are to rehabilitate and reintegrate individuals with PCC back into society and/or employment.\textsuperscript{4} We would, therefore, like to end this commentary by quoting the authors' 2 concluding sentences from their article: “However, given that exercise was generally well tolerated, guidelines cautioning against exercise in similar populations may need to be revised. It seems advisable to cautiously incorporate exercise into rehabilitation protocols and adjust the intensity progressively, considering patients' symptoms and abilities.”\textsuperscript{2}
ARTICLE INFORMATION

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