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Adapted Physical Activity Protocol Improves Health-Related Quality of Life and Psychological Outcomes in Long COVID: A Prospective Longitudinal Study

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Background: Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, has resulted in persistent symptoms in some individuals—referred to as long COVID or post-acute sequelae of SARS-CoV-2 infection (PASC). Common symptoms such as fatigue, dyspnea, anxiety, and depression can markedly impair health-related quality of life (HRQOL). Conventional rehabilitation may be insufficient, raising interest in Adapted Physical Activity (APA) as a non-pharmacological strategy to improve physical and psychological outcome. Thus, this study aimed to evaluate the short- and medium-term effects of an APA protocol on HRQOL and psychological outcomes in patients with long COVID.

Methods: Fifty non-hospitalized patients with long COVID (mean age 52.0 ± 15.3 years; 44% female) participated in in a prospective, longitudinal observational study. Each patient underwent a 6-week APA program consisting of two 30-minute individualized cardiorespiratory sessions per week. HRQOL (SF-12), anxiety, and depression (HADS) were evaluated at baseline (E1), immediately post-intervention (E2), and at 5–7 months follow-up (E3).

Results: Significant improvements were found in both physical and mental SF-12 scores across time points ($p < 0.001$). The proportion of patients with normal physical HRQOL rose from 16% at baseline to 90% at E2 and remained higher than baseline at E3 (66%). Symptoms of anxiety and depression were significantly reduced ($p < 0.001$). Dyspnea prevalence decreased substantially from baseline to follow-ups. Strong negative correlations were observed between HRQOL and HADS scores ($p < 0.001$).

Conclusion: The APA protocol showed significant short- and medium-term improvements in HRQOL and psychological outcomes in long COVID patients. Benefits were more pronounced for physical symptoms and anxiety than for depression. These findings suggest that structured physical activity may offer a feasible, non-pharmacological strategy to enhance recovery and quality of life. Incorporating APA into routine care may help meet the diverse functional and psychological needs of this population.

Keywords: anxiety, cardiorespiratory fitness, depression, Post-COVID Syndrome, quality of life, COVID-19 Rehabilitation

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Contributions to the Literature

- This study demonstrates the effectiveness of Adapted Physical Activity (APA) protocols as a non-pharmacological intervention for managing physical and psychological sequelae of long COVID.
- It provides robust evidence of significant short- and medium-term improvements in health-related quality of life (HRQOL), anxiety, and depression.
- The study emphasizes the value of individualized rehabilitation strategies to address the diverse needs of long COVID patients.
- Findings advocate for integrating structured exercise programs into routine care to enhance recovery and reduce healthcare burdens.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in unprecedented global health challenges.[1–3] While acute COVID-19 has been extensively studied, increasing attention is now focused on the long-term sequelae of the infection, commonly referred to as "long COVID" or "post-acute sequelae of SARS-CoV-2 infection" (PASC).[4] Long COVID is characterized by persistent symptoms and functional impairments that extend beyond the acute phase of infection, often lasting for months.[5,6]

The prevalence of long COVID varies across studies, with estimates ranging from 10% to 30% of individuals who have had COVID-19.[7] A systematic review by Lopez-Leon et al,[8] identified 55 long-term effects of COVID-19, with fatigue, headache, attention disorder, hair loss, and dyspnea being the most common. The heterogeneity in reported prevalence and symptom profiles underscores the complex nature of long COVID and the challenges in its diagnosis and management. Long COVID affects multiple organ systems, with symptoms spanning respiratory, cardiovascular, neurological, and psychological domains.[9] Respiratory symptoms, such as persistent dyspnea and reduced exercise tolerance, are particularly common and can significantly impact patients' quality of life.[10] Neurological and cognitive symptoms, often referred to as "brain fog", include difficulties with memory, concentration, and executive function.[11] Additionally, a high prevalence of mental health issues, including anxiety and depression, has been reported in long COVID patients.[12] This is consistent with findings from clinical populations, where elevated levels of anxiety, depression, and post-traumatic stress symptoms have been documented among COVID-19 survivors.[13] The pathophysiology of long COVID remains incompletely understood. Proposed mechanisms include persistent viral reservoirs, autoimmune phenomena, and dysregulated inflammatory responses.[14]

Health-related quality of life (HRQOL) is increasingly recognized as a crucial outcome measure in long COVID research and clinical practice.[15] Studies have consistently shown that long COVID patients experience significant reductions in HRQOL across physical, mental, and social domains.[16] In this prospective cohort study conducted across 17 countries,[17] including both high-income and low-to-middle-income countries, researchers found that a significant proportion of COVID-19 survivors experienced persistent symptoms like fatigue, breathlessness, and cognitive dysfunction up to 12 months post-hospital discharge.[18] These symptoms were associated with reduced quality of life and daily functioning.[17] The impact of long-term COVID-19 on HRQOL extends beyond the individual patient, affecting families, communities, and healthcare systems.[19] Many long COVID patients struggle to return to work or maintain pre-illness levels of productivity, leading to significant economic consequences.[20]

Given the diverse and persistent nature of long COVID symptoms, there is a growing recognition of the need for comprehensive rehabilitation strategies.[21] Rehabilitation interventions aim to address the multi-system effects of long-term COVID-19, improve functional capacity, and enhance overall quality of life.[22] However, the optimal approach to long COVID rehabilitation remains a subject of ongoing research and debate. Standard rehabilitation for Long COVID typically involves pulmonary training for respiratory function and fatigue, as well as cognitive therapy for neurocognitive impairments. In contrast, Adapted Physical Activity (APA) offers a more comprehensive, personalized approach by combining aerobic, respiratory, and strength training to address both physical and psychological sequelae. This integrative method enhances the potential for scalable, individualized recovery within the broader rehabilitation framework.[23] In addition, physical activity and exercise-based interventions have shown promise in addressing many

of the symptoms associated with long COVID.[24] A systematic review by Torres and Gradidge[25] highlighted the potential benefits of exercise in improving cardiorespiratory fitness, muscle strength, and fatigue in post-COVID-19 patients. However, concerns about post-exertional symptom exacerbation have led to calls for caution and individualized approaches to exercise prescription in this population.[26] APA protocols represent a tailored approach to rehabilitation that considers the unique challenges faced by long COVID patients.[27] These protocols typically incorporate a combination of aerobic exercise, strength training, and respiratory exercises, with careful monitoring and progression based on individual patient responses.[27,28]

The high prevalence of mental health issues in long COVID patients highlights the need for integrated psychological interventions.[27] Anxiety and depression not only impact quality of life but may also exacerbate physical symptoms and hinder recovery.[29] Cognitive-behavioral therapy (CBT) and mindfulness-based interventions have shown efficacy in managing chronic illness symptoms and may be beneficial for long-term COVID patients.[30] Moreover, the uncertain prognosis and often invisible nature of long COVID symptoms can lead to feelings of frustration, isolation, and lack of validation.[31]

Recent evidence shows that structured APA effectively reduces anxiety and depression in long COVID patients, thanks to its physiological, cognitive, and social benefits.[32] Combining personalized aerobic and respiratory training, APA supports both physical recovery and psychological resilience by modulating stress and enhancing self-efficacy.[33] These findings support its integration into multidisciplinary post-COVID care.

Despite the growing body of research on long COVID, significant knowledge gaps remain. The natural history of the condition, including the trajectory of symptom resolution and potential for full recovery, is not yet fully understood.[34] There is also a need for well-designed, controlled studies evaluating the efficacy of various rehabilitation approaches for long COVID.[35] While early evidence supports the use of exercise-based interventions, questions remain regarding the optimal timing, intensity, and duration of such programs.[36] The long-term impact of COVID-19 on healthcare systems and society at large is another area requiring ongoing research.[37]

The present study aims to address this gap by investigating the short- and medium-term impacts of an APA protocol on health-related quality of life and psychological outcomes in patients with long-term COVID.

Material and Methods

Study Design

This single-center, prospective, longitudinal observational study included 50 patients (mean age 52.0 ± 15.3 years; 44% female) with long COVID and was conducted at the Physical Medicine and Rehabilitation Department of Mohamed Kassab Institute of Orthopedics, Manouba, Tunisia, from June 2020 to March 2022, at the beginning of May 2020. The study protocol was approved by the institutional ethics committee of the National Institute of Orthopedy Mohamed KASSAB under the reference (IMKO-CE-2022-2), and conducted by the Declaration of Helsinki. It also complied with the highest ethical and procedural requirements of the conduct of sports medicine and exercise science research as outlined by Guelmemi et al.[38] All participants provided written informed consent before enrollment.

Participants

The sample size was calculated using G*Power 3.1 software.[39] Assuming a medium effect size of 0.5, alpha of 0.05, and power of 0.80 for repeated measures ANOVA with 3-time points, the required sample size was 28 participants. Accounting for potential attrition, we aimed to recruit 50 participants.

Patients with long COVID-19 referred for cardiorespiratory rehabilitation were eligible for inclusion. Long COVID was defined as the presence of symptoms persisting for at least 4 weeks after acute SARS-CoV-2 infection. Inclusion criteria were: 1) age 18–85 years, 2) symptoms meeting the definition of long COVID, 3) no contraindications to exercise, and 4) ability to provide informed consent. Exclusion criteria were: oxygen dependence, cognitive/psychiatric impairment affecting evaluation accuracy, pregnancy, and unwillingness to participate.

Procedures

Eligible participants underwent baseline assessment (E1) before beginning a 6-week individualized outpatient APA protocol. The protocol consisted of two 30-minute sessions per week, incorporating respiratory training, bronchial decongestion, and exercise rehabilitation tailored to each patient's cardiorespiratory needs. Exercise intensity was progressively adjusted throughout the intervention period. Participants were instructed to maintain their usual diet and physical activity levels outside of the intervention sessions. They were encouraged to attend all sessions and complete home exercises as prescribed. Adherence was monitored through attendance logs and exercise diaries.

Follow-up assessments were conducted immediately post-intervention (E2) and 5–7 months post-intervention (E3). All evaluations were conducted in a quiet, temperature-controlled room by the same experienced evaluator blinded to previous results. Participants were asked to avoid caffeine, alcohol, and strenuous exercise for 24 hours before testing. Verbal encouragement was provided during physical assessments to elicit maximal effort.

Measurements

Demographic data, medical history, anthropometrics, and COVID-19 illness characteristics were collected at baseline. The following outcome measures were assessed at E1, E2, and E3.

Health-Related Quality of Life

Health-related quality of life was assessed using the 12-Item Short Form Health Survey (SF-12), a shortened version of the SF-36 developed by the RAND Corporation and John E. Ware Jr. The SF-12 measures health-related quality of life through eight domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. These domains are combined into two composite scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). The scoring method uses a norm-based algorithm, with a mean of 50 and a standard deviation of 10, allowing for comparisons across populations. Higher scores reflect better health status. The SF-12 has been validated in numerous studies, with Cronbach's alpha values typically exceeding 0.80, indicating high reliability. Its validity has been confirmed through strong correlations with the SF-36 and other quality-of-life measures. It is widely used in both clinical and research settings, particularly for populations with chronic conditions like cancer, diabetes, and respiratory diseases.[40]

Dyspnea

The degree of breathlessness was assessed using the Modified Medical Research Council (mMRC) Dyspnea Scale, developed by the Medical Research Council in the UK. This tool is a simple, patient-reported scale that evaluates dyspnea on a five-point scale from 0 to 4, with higher scores indicating more severe breathlessness. The mMRC scale is commonly used in clinical practice and research to assess functional impairment in patients with chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). It has shown good reliability, with inter-rater and test-retest reliability coefficients exceeding 0.70 in validation studies. Furthermore, it is correlated with objective measures of lung function, such as FEV_1, and quality-of-life tools, providing strong evidence for its validity. Its simplicity and ease of administration make it a practical tool for routine assessments.[41]

Psychological Status

Psychological status was measured using the Hospital Anxiety and Depression Scale (HADS), a widely used screening tool developed by Zigmond and Snaith in 1983 to identify anxiety and depression in hospital settings. The HADS consists of 14 items divided into two subscales: anxiety (HADS-A) and depression (HADS-D), each containing seven items. Responses are scored on a 4-point Likert scale (0–3), resulting in subscale scores ranging from 0 to 21. Scores of 8–10 are considered borderline abnormal, and scores of 11 or above suggest clinical anxiety or depression. The HADS has been extensively validated across different populations, including general medical, surgical, and psychiatric patients. It demonstrates excellent internal consistency, with Cronbach's alpha values ranging from 0.80 to 0.93, and has strong construct validity, as evidenced by its correlations with other measures of psychological distress, such as the Beck Depression Inventory and State-Trait Anxiety Inventory.[42]

Functional Capacity

Functional capacity was assessed using the Six-Minute Walk Test (6MWT), a standardized exercise test that measures the distance an individual can walk in six minutes on a flat, hard surface. The 6MWT was developed as part of pulmonary rehabilitation programs and is endorsed by the American Thoracic Society (ATS). It reflects an individual's ability to perform daily physical activities and is particularly useful for evaluating patients with cardiopulmonary diseases, heart failure, and other chronic conditions. The test is conducted under controlled conditions with standardized instructions, and participants are allowed to rest as needed during the test. The total distance walked is recorded in meters. The 6MWT has excellent test-retest reliability (ICC > 0.90) and is strongly correlated with peak oxygen uptake (VO_2 max) and other measures of functional capacity, confirming its validity. It is sensitive to changes in physical fitness and has prognostic value for morbidity and mortality in chronic diseases.[43]

Respiratory Function

Respiratory function was evaluated using spirometry, focusing on two key parameters: Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 Second (FEV_1). Spirometry is the gold standard for assessing pulmonary function and diagnosing respiratory disorders. FVC represents the total volume of air that can be forcibly exhaled after a full inhalation, while FEV_1 measures the volume of air exhaled during the first second of the forced expiratory maneuver. These values are typically expressed as percentages of predicted values based on age, sex, height, and ethnicity. The ratio of FEV_1 to FVC (FEV_1/FVC) is a critical indicator of obstructive or restrictive lung diseases. Spirometry has demonstrated excellent reliability (ICC > 0.95) and validity in detecting respiratory abnormalities, with widespread use in clinical and research settings. Calibration of the spirometer and adherence to standardized testing protocols are essential for ensuring accurate measurements.[44]

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). The Shapiro–Wilk test was used to assess the normality of data distribution. Descriptive statistics were calculated as frequencies and percentages for categorical variables, mean ± standard deviation for normally distributed continuous variables, and median (interquartile range) for non-normally distributed continuous variables. Changes in outcomes across the three-time points (E1, E2, E3) were analyzed using Friedman test for non-parametric repeated measures. Post-hoc analyses were conducted using Wilcoxon signed-rank tests with Bonferroni correction for multiple comparisons. Associations between variables were examined using Spearman's rank correlation coefficient (rs). Correlation strength was interpreted as weak (0–0.299), moderate (0.300–0.499), or strong (0.500–1.000).[45] Simple linear regression was performed to assess linearity, with R^2 values interpreted similarly. Group comparisons were conducted using Mann–Whitney *U*-tests for continuous variables and Chi-square tests for categorical variables. The Kruskal–Wallis *H*-test was used for comparisons between multiple groups. Effect sizes were calculated using partial eta squared (η^2_p) for Friedman test (small: 0.01–0.05, medium: 0.06–0.13, large: ≥0.14)[46] and r for Wilcoxon signed-rank tests and Mann–Whitney *U*-tests (small: 0.10–0.29, medium: 0.30–0.49, large: ≥0.50).[47] A two-tailed p-value <0.05 was considered statistically significant. To account for potential confounding factors, multivariate linear regression analyses were performed to assess the independent effects of the APA intervention on psychological outcomes (HADS-A and HADS-D) at E2 and E3, adjusting for age, sex, BMI, disease severity, and smoking status.

Results

Fifty patients with long-term COVID-19 completed the study protocol. The cohort had a mean age of 52.0±15.3 years and a male-to-female ratio of 1.27. Most participants (52%) had university-level education, and 82% were non-smokers. The mean BMI was 30.74±4.35 kg/m^2, indicating a predominantly obese population (Table 1). Baseline comparisons between smokers and non-smokers showed no statistically significant differences in age (p = 0.80), BMI (p = 0.44), sex distribution (p = 0.35), or disease severity (p = 0.19), indicating a relatively balanced sample across key demographic and clinical variables.

Table 1 Demographic Data of the Population

Demographic Data	n=50
Age (years-old)	52.0±15.3
Female gender	22 (44%)
BMI (Kg/m^2)	30.74 ± 4.35
Education (n, %)	
Primary	7 (14%)
Secondary	12 (24%)
University	26 (52%)
Tobacco (n, %)	
Smoking	9 (18%)
Non-smoking	41 (82%)

Comorbidities were prevalent, with diabetes (24%) and hypertension (22%) being most common. The severity of initial COVID-19 infection was classified as mild (48%), moderate (24%), or severe (28%). Nearly half of the patients (48%) required hospitalization, with 20% admitted to intensive care units. The median hospital stay was 20 days (range: 2–65) (Table 2).

At baseline, 43 patients (86%) reported dyspnea based on the mMRC scale. Following the APA protocol, dyspnea prevalence significantly decreased at E2 (n=26, 52%; $p<0.001$) and E3 (n=21, 42%; $p<0.001$), representing a 51.2% reduction from baseline to medium-term follow-up (Table 3).

The SF-12 physical component score (PCS) showed significant improvements across time points ($\chi^2(2)=73.24$, $p<0.001$, $\eta^2_p=0.73$). Normal physical HRQOL increased from 16% at baseline to 90% at E2 ($p=0.017$, $r=0.34$) and 66% at E3 ($p=0.012$, $r=0.35$). The median PCS improved from 35.5 (IQR: 30.25–41.75) at E1 to 48.0 (IQR: 44.0–52.0) at E2 and 46.0 (IQR: 41.0–50.0) at E3. Similarly, the SF-12 mental component score (MCS) improved significantly ($\chi^2(2)=68.92$, $p<0.001$, $\eta^2_p=0.69$). Normal mental HRQOL increased from 18% at baseline to 86% at E2 ($p<0.001$, $r=0.62$) and 66% at E3 ($p<0.001$, $r=0.55$). The median MCS improved from 36.0 (IQR: 31.0–42.0) at E1 to 49.0 (IQR: 45.0–53.0) at E2 and 47.0 (IQR: 42.0–51.0) at E3 (Table 3).

Anxiety symptoms (HADS-A) improved significantly over time ($\chi^2(2) = 61.78$, $p<0.001$, $\eta^2_p=0.62$). The proportion of patients with normal anxiety scores increased from 26% at baseline to 82% at E2 ($p<0.001$, $r=0.58$) and 56% at E3 ($p<0.001$, $r=0.50$). The median HADS-A score decreased from 10 (IQR: 7–13) at E1 to 6 (IQR: 4–8) at E2 and 7 (IQR: 5–9) at E3. Depression symptoms (HADS-D) also improved significantly ($\chi^2(2)=55.36$, $p<0.001$, $\eta^2_p=0.55$). The

Table 2 Distribution of Comorbidities and Their Association with Outcomes

Comorbidities	n (%)	Association with HRQOL (SF-12)	Association with HAD
Diabetes	12 (24%)	$r = -0.25$, $p = 0.08$	$r = 0.22$, $p = 0.12$
Hypertension	11 (22%)	$r = -0.20$, $p = 0.16$	$r = 0.18$, $p = 0.21$
Dyslipidemia	5 (10%)	$r = -0.15$, $p = 0.30$	$r = 0.12$, $p = 0.40$
Coronary artery disease	3 (6%)	$r = -0.18$, $p = 0.21$	$r = 0.16$, $p = 0.27$
Asthma	2 (4%)	$r = -0.10$, $p = 0.49$	$r = 0.09$, $p = 0.53$
Epilepsy	2 (4%)	$r = -0.08$, $p = 0.58$	$r = 0.07$, $p = 0.63$
Chronic bronchitis	1 (2%)	$r = -0.05$, $p = 0.73$	$r = 0.04$, $p = 0.78$
Stroke	1 (2%)	$r = -0.06$, $p = 0.68$	$r = 0.05$, $p = 0.73$

Note: p: statistical significance (p value).
Abbreviations: r, Spearman's rank correlation coefficient; HRQOL, Health-Related Quality of Life; HAD, Hospital Anxiety and Depression Scale; n (%), number and percentage.

Table 3 Distribution of COVID-19 Data and Their Impact on Outcomes

COVID-19 Data	n (%)	Impact on HRQOL (SF-12)	Impact on HAD
***Severity* (n, %)**		χ^2 = 8.24, p = 0.016	χ^2 = 7.56, p = 0.023
Mild	24 (48%)	Ref	Ref
Moderate	12 (24%)	β = −0.22, p = 0.04	β = 0.20, p = 0.06
Severe	14 (28%)	β = −0.35, p = 0.001	β = 0.33, p = 0.002
***Care environment* (n, %)**		F = 12.35, p < 0.001	F = 10.78, p < 0.001
Home care	26 (52%)	Ref	Ref
Hospital care	24 (48%)	β = −0.30, p = 0.002	β = 0.28, p = 0.005
Medical department	14 (28%)	β = −0.25, p = 0.01	β = 0.23, p = 0.02
Intensive care unit	10 (20%)	β = −0.38, p < 0.001	β = 0.36, p < 0.001
Length of hospital stays (days)	20 [2–65]	r = −0.42, p < 0.001	r = 0.40, p < 0.001
Signs and symptoms of long COVID (n, %)			
Effort dyspnea	33 (66%)	β = −0.45, p < 0.001	β = 0.42, p < 0.001
Rest dyspnea	12 (24%)	β = −0.38, p < 0.001	β = 0.36, p < 0.001
Dry cough	15 (30%)	β = −0.20, p = 0.04	β = 0.18, p = 0.07
Myalgia	13 (26%)	β = −0.22, p = 0.03	β = 0.20, p = 0.05
Memory disorders	10 (20%)	β = −0.28, p = 0.005	β = 0.26, p = 0.009

Notes: The severity of COVID-19 was classified based on clinical presentation and care requirements during the acute phase, following WHO guidelines, Mild (symptomatic patients without evidence of pneumonia or hypoxia); Moderate (clinical signs of pneumonia (fever, cough, dyspnea) but no signs of severe pneumonia); Severe (patients requiring hospitalization with respiratory distress, oxygen saturation < 90%, or Intensive Care Unit admission).

Abbreviations: χ^2, Chi-square test statistic; F, F-statistic from ANOVA; β, Standardized regression coefficient; r, Spearman's rank correlation coefficient; Ref, Reference category; HRQOL, Health-Related Quality of Life; HAD, Hospital Anxiety and Depression Scale.

proportion of patients with normal depression scores increased from 24% at baseline to 66% at E2 (p<0.001, r=0.52) and 52% at E3 (p<0.001, r=0.46). The median HADS-D score decreased from 9 (IQR: 7–11) at E1 to 5 (IQR: 3–7) at E2 and 6 (IQR: 4–8) at E3 (Table 3).

A significant negative correlation was found between global SF-12 scores and the mMRC dyspnea scale at E1 (rs= −0.38, p=0.006) and E3 (rs=−0.34, p=0.016). Non-smokers had higher SF-12 physical scores at E1 (U=107.5, p=0.035, r=0.30) and mental scores at E3 (U=115.0, p=0.048, r=0.28) compared to smokers. Smokers exhibited significantly higher depression (U=110.5, p=0.039, r=0.29) and anxiety scores (U=89.5, p=0.01, r=0.36) compared to non-smokers. Strong negative correlations were observed between SF-12 scores (global, mental, and physical) and HADS scores (anxiety and depression) across all time points (all p<0.001, rs ranging from −0.45 to −0.72) (Table 4). Multivariate regression models did not identify any single baseline factor as a statistically significant predictor of HADS-A or HADS-

Table 4 Study of the Association Between SF-12 and HAD in the Three Assessments

	Measures				
	E1	**E2**	**E3**	η^2_p	***p*-value**
SF-12 Global	35.2 ± 8.7	48.6 ± 7.2	46.8 ± 7.8	0.68	<0.0001
SF-12 Physical	35.5 ± 9.1	48.0 ± 6.9	46.0 ± 7.5	0.73	<0.0001
SF-12 Mental	36.0 ± 8.5	49.0 ± 7.4	47.0 ± 7.7	0.69	<0.0001
HAD-A	10.2 ± 4.3	6.1 ± 3.2	7.3 ± 3.6	0.62	<0.0001
HAD-D	9.4 ± 3.9	5.3 ± 2.8	6.2 ± 3.1	0.55	<0.0001

(*Continued*)

Table 4 (Continued).

Associations			
	E1 (rs)	**E2 (rs)**	**E3 (rs)**
SF12 Global / HAD-A	−0.68**	−0.72**	−0.70**
SF12 Global / HAD-D	−0.65**	−0.69**	−0.67**
SF12 Physical / HAD-A	−0.62**	−0.66**	−0.45**
SF12 Physical / HAD-D	−0.60**	−0.64**	−0.62**
SF12 Mental / HAD-A	−0.58**	−0.70**	−0.68**
SF12 Mental / HAD-D	−0.63**	−0.68**	−0.66**

Note: **Correlation is significant at the 0.01 level (2-tailed).
Abbreviations: E1, baseline assessment; E2, short-term assessment (immediately post-rehabilitation); E3, medium-term assessment (5–7 months post-rehabilitation); HAD-A, Hospital Anxiety and Depression Scale - Anxiety subscale; HAD-D, Hospital Anxiety and Depression Scale - Depression subscale; η^2_p, partial eta squared (effect size for repeated measures ANOVA); rs, Spearman's rank correlation coefficient.

D scores at follow-up (all $p > 0.05$), suggesting that the observed improvements were not confounded by demographic or clinical variables.

Discussion

This study investigated the short- and medium-term effects of an APA protocol on health-related quality of life (HRQOL) and psychological outcomes in patients with long-term COVID-19. Our findings demonstrated significant improvements in both physical and mental aspects of HRQOL, as well as reductions in anxiety and depression symptoms, following the implementation of the APA protocol.

The SF-12 physical component score (PCS) showed substantial improvements across the study period ($\chi^2(2)=73.24$, $p<0.001$, $\eta^2_p=0.73$), with the proportion of patients reporting normal physical HRQOL increasing from 16% at baseline to 90% immediately post-intervention and 66% at medium-term follow-up. These findings are consistent with recent studies on rehabilitation interventions for long COVID patients. For instance, Daynes et al[48] reported significant improvements in physical function following a 6-week rehabilitation program, with patients demonstrating enhanced exercise capacity and reduced fatigue. The observed improvements in physical HRQOL may be attributed to several factors. Firstly, the APA protocol likely contributed to improved cardiovascular fitness and muscular strength, which are often compromised in long COVID patients.[27] Additionally, the structured exercise program may have helped address the deconditioning that frequently occurs during prolonged illness and inactivity.[36] The gradual progression of exercise intensity in our protocol aligns with current recommendations for post-COVID rehabilitation, which emphasize the importance of individualized, graded exercise to avoid symptom exacerbation.[49] Similarly, the SF-12 mental component score (MCS) showed significant improvements ($\chi^2(2)=68.92$, $p<0.001$, $\eta^2_p=0.69$), with the proportion of patients reporting normal mental HRQOL increasing from 18% at baseline to 86% post-intervention and 66% at medium-term follow-up. This finding emphasizes the potential of physical activity interventions to positively impact mental well-being in long COVID patients. The psychological benefits of exercise are well-documented in various clinical populations,[50] and our results suggest that these benefits extend to individuals recovering from COVID-19. The improvement in mental HRQOL may be explained by several mechanisms. Exercise has been shown to reduce inflammation and oxidative stress, which are implicated in the pathophysiology of both COVID-19 and mental health disorders.[51]

Our study revealed significant reductions in both anxiety ($\chi^2(2)=61.78$, $p<0.001$, $\eta^2_p=0.62$) and depression symptoms ($\chi^2(2)=55.36$, $p<0.001$, $\eta^2_p=0.55$) following the APA protocol. The proportion of patients with normal anxiety scores increased from 26% at baseline to 82% post-intervention and 56% at medium-term follow-up. Similarly, the proportion of patients with normal depression scores increased from 24% at baseline to 66% post-intervention and 52% at medium-term follow-up. These findings align with emerging evidence on the psychological impact of long COVID and the

potential benefits of rehabilitation interventions. An umbrella review by Witteveen et al[52] highlighted the high prevalence of anxiety and depression among COVID-19 survivors, emphasizing the need for targeted interventions to address these mental health concerns. Our results suggest that structured physical activity programs may be an effective non-pharmacological approach to managing psychological symptoms in this population. The observed improvements in anxiety and depression symptoms may be attributed to several factors. Exercise has been shown to modulate neurotransmitter systems, including serotonin and norepinephrine, which play crucial roles in mood regulation.[53] Additionally, the social interaction and support provided during group-based rehabilitation sessions may have contributed to improved psychological well-being.[54]

These psychological improvements are further supported by existing literature emphasizing the role of structured physical activity in post-COVID rehabilitation. Witteveen et al[52] highlighted the urgent need for targeted mental health interventions among COVID-19 survivors, while Mahindru et al[50] and Alizadeh Pahlavani[53] demonstrated that exercise can positively influence mood through neurochemical and anti-inflammatory mechanisms. The sustained reductions in anxiety and depression observed in our cohort at both short- and medium-term follow-ups reinforce the therapeutic value of APA. Moreover, the strong inverse correlations between HRQOL and HADS scores across all time points (Table 4) underscore the interdependence of physical and psychological recovery. These findings advocate for the integration of APA into comprehensive rehabilitation strategies to address the persistent mental health burden associated with long COVID.

Additionally, our study demonstrated a significant reduction in dyspnea prevalence following the APA protocol, with the number of patients reporting dyspnea decreasing from 86% at baseline to 52% post-intervention and 42% at medium-term follow-up. This improvement in respiratory symptoms is consistent with other studies on post-COVID rehabilitation. For example, Nopp et al[55] reported significant improvements in dyspnea and exercise capacity following a 3-week pulmonary rehabilitation program in COVID-19 survivors. The reduction in dyspnea may be attributed to several mechanisms. Firstly, the respiratory training component of our APA protocol likely improved respiratory muscle strength and endurance, potentially enhancing ventilatory efficiency.[56] Secondly, the aerobic exercise component may have improved overall cardiovascular fitness, leading to better oxygen utilization and reduced perceived breathlessness during daily activities.[57] Additionally, the education and breathing technique training provided as part of the protocol may have enhanced patients' self-management skills and confidence in managing their respiratory symptoms.[58] The observed negative correlation between global SF-12 scores and mMRC dyspnea scale ($rs=-0.38$ at E1, $rs=-0.34$ at E3, both $p<0.05$) highlights the significant impact of respiratory symptoms on overall quality of life in long-term COVID patients. This finding underscores the importance of addressing dyspnea as a key component of long-term COVID-19 rehabilitation programs.

Our study identified several factors that influenced HRQOL and psychological outcomes in long COVID patients. Notably, smoking status was significantly associated with both physical and mental HRQOL, with non-smokers demonstrating higher SF-12 scores compared to smokers. This finding is consistent with previous research on the negative impact of smoking on COVID-19 outcomes and recovery.[59] The detrimental effects of smoking on lung function and overall health may exacerbate the respiratory and systemic symptoms experienced by long COVID-19 patients, potentially hindering their recovery and quality of life.[60] Furthermore, we observed strong negative correlations between SF-12 scores and HADS scores across all time points (*rs* ranging from −0.45 to −0.72, all $p<0.001$). This robust association between HRQOL and psychological symptoms underscores the interconnected nature of physical and mental well-being in long COVID patients. It suggests that interventions targeting both physical and psychological aspects of recovery may be more effective than those focusing on a single domain.[61] The severity of initial COVID-19 infection and the need for hospitalization were also associated with poorer outcomes in our study. This finding aligns with previous research indicating that patients with more severe acute illness are at higher risk of developing long-term complications and experiencing a more prolonged recovery.[62] Additionally, the demographic characteristics of our cohort, notably the predominance of obesity (mean BMI 30.74 ± 4.35 kg/m²) and older age (mean age 52.0 ± 15.3 years), may have influenced the outcomes. These factors are known to contribute to prolonged recovery and reduced physical function post-COVID-19. Therefore, the observed improvements in HRQOL and psychological outcomes may reflect the responsiveness of these subgroups to structured physical activity interventions.

Despite the promising findings, this study has several limitations that should be acknowledged. First, the absence of a control group limits the ability to draw definitive causal inferences regarding the effects of the APA intervention. Although multivariate regression was used to adjust for potential confounders, randomized controlled trials are needed to confirm these associations. Second, our study relied heavily on self-reported survey data, which may introduce response bias and affect the objectivity of the findings. Lastly, while the APA protocol was individualized, further research is needed to determine the optimal components and dosage of exercise for different subgroups of long COVID patients.[63] Furthermore, although the Six-Minute Walk Test (6MWT) is a validated and practical tool for assessing functional capacity, it is not the gold standard for evaluating cardiorespiratory fitness. Cardiopulmonary Exercise Testing (CPET) is considered the reference method for directly measuring VO_2max. Future studies should incorporate CPET, as demonstrated in the NOODLE study,[64] to provide more accurate assessments of aerobic capacity and training effects.

Implications for Clinical Practice and Future Research

Our findings affect long-term COVID clinical care in numerous ways. It is also important to note that our sample consisted predominantly of older adults with obesity, which may have influenced both baseline impairments and the magnitude of improvements observed. These characteristics are known to affect recovery trajectories and should be considered when interpreting the results. Individualized structured physical exercise programs improve physical and mental health holistically. These treatments may help long-term COVID-19 patients with physical restrictions, anxiety, and depression. Healthcare providers managing long-term COVID patients should implement personalized physical activity programs, incorporate aerobic and respiratory training, regularly assess and monitor symptoms, support smoking cessation, tailor rehabilitation intensity, and provide ongoing support and follow-up. Long-term COVID-19 rehabilitation procedures should be improved in future studies. This involves studying the best timing, duration, and intensity of exercise treatments and the advantages of combining physical activity with other therapies. Long-term rehabilitation program studies are required to measure lasting gains and advise continuing support tactics.

Conclusions

This study demonstrates that an APA program can significantly enhance HRQOL and psychosocial outcomes in patients with long-term COVID-19, improving both physical and mental health metrics. Personalized APA interventions appear to alleviate somatic symptoms and anxiety, noticeably improving general wellness in these individuals. Further, the findings indicate that smoking status and the severity of dyspnea are key factors that influence recovery, underlining the importance of tailored follow-up care. Although the absence of a control group and the small sample size limit the generalizability of these findings, the observed benefits suggest that APA could be a valuable clinical intervention. Structured physical activities emerge as a promising non-pharmacological approach, though larger randomized controlled trials are needed to confirm these early results. Integrating personalized APA into standard care for long COVID may enhance both physical and psychological outcomes, offering hope for people facing persistent post-COVID symptoms.

Data Sharing Statement

Data are available from the first author upon reasonable request.

Ethics Approval and Consent to Participate

The institutional ethics committee of the National Institute of Orthopedy Mohamed KASSAB approved the study protocol under the reference (IMKO-CE-2022-2) at the beginning of May 2020 and conducted it following the Declaration of Helsinki. Participants gave written informed consent to participate in the present study and its publication.

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Disclosure

All authors declare no conflicts of interest in this work.

References

1. Musa S, Dergaa I, Bachiller V, Saad HB. Global Implications of COVID-19 pandemic on adults' lifestyle behavior: the invisible pandemic of noncommunicable disease. *Int J Prev Med*. 2023;14:15. doi:10.4103/ijpvm.ijpvm_157_21
2. Varma A, Dergaa I, Mohammed AR, et al. Covid-19 and diabetes in primary care - How do hematological parameters present in this cohort? *Expert Rev Endocrinol Metab*. 2021;16(3):147-53. doi:10.1080/17446651.2021.1909472
3. Dergaa I, Ammar A, Souissi A, et al. COVID-19 lockdown: impairments of objective measurements of selected physical activity, cardiorespiratory and sleep parameters in trained fitness coaches. *EXCLI J*. 2022;21:1084-98. doi:10.17179/excli2022-4986
4. Wang C, Ramasamy A, Verduzco-Gutierrez M, Brode WM, Melamed E. Acute and post-acute sequelae of SARS-CoV-2 infection: a review of risk factors and social determinants. *Virol J*. 2023;20:124. doi:10.1186/s12985-023-02061-8
5. Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol*. 2023;21:133-46.
6. Souissi A, Dergaa I, Romdhani M, et al. Can melatonin reduce the severity of post-COVID-19 syndrome? *Excli J*. 2023;22:173-87. doi:10.17179/excli2023-5864
7. Woodrow M, Carey C, Ziauddeen N, et al. Systematic Review of the Prevalence of Long COVID. *Open Forum Infect Dis*. 2023;10:233. doi:10.1093/ofid/ofad233
8. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al. More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis. *Sci. Rep*. 2021;11;(1):16144
9. Rathod N, Kumar S, Chavhan R, Acharya S, Rathod S. Navigating the long haul: a comprehensive review of long-COVID sequelae, patient impact, pathogenesis, and management. *Cureus*. 2024;16:60176.
10. Vogelmeier CF, Román-Rodríguez M, Singh D, Han MK, Rodríguez-Roisin R, Ferguson GT. Goals of COPD treatment: focus on symptoms and exacerbations. *Respir Med*. 2020;166:105938. doi:10.1016/j.rmed.2020.105938
11. Krishnan K, Lin Y, Prewitt KM, Potter DA. Multidisciplinary approach to brain fog and related persisting symptoms post COVID-19. *J Health Serv Psychol*. 2022;48:31-8.
12. Zhang Y, Chinchilli VM, Ssentongo P, Ba DM. Association of Long COVID with mental health disorders: a retrospective cohort study using real-world data from the USA. *BMJ Open*. 2024;14:079267.
13. Kasiak PS, Adamczyk N, Jodczyk AM, et al. COVID-19 pandemic consequences among individuals with eating disorders on a clinical sample in poland-a cross-sectional study. *Int J Environ Res Public Health*. 2022;19(14):8484. doi:10.3390/ijerph19148484
14. Bohmwald K, Diethelm-Varela B, Rodríguez-Guilarte L, et al. Pathophysiological, immunological, and inflammatory features of long COVID. *Front Immunol*. 2024;15:1341600.
15. Amdal CD, Taylor K, Kuliś D, et al. Health-related quality of life in patients with COVID-19; international development of a patient-reported outcome measure. *J Patient Rep Outcomes*. 2022;6:26. doi:10.1186/s41687-022-00434-1
16. Mahony L O, Buwalda T, Blair M, et al. Impact of Long COVID on health and quality of life. *HRB Open Res*. 2022;5:31. doi:10.12688/hrbopenres.13516.1
17. Pazukhina E, Garcia-Gallo E, Reyes LF, et al. Long Covid: a global health issue–a prospective, cohort study set in four continents. *BMJ Global Health*. 2024;9(10):015245.
18. Śliż D, Wiecha S, Gąsior JS, et al. The Influence of Nutrition and Physical Activity on Exercise Performance after Mild COVID-19 Infection in Endurance Athletes-CESAR Study. *Nutrients*. 2022;14(24):5381. doi:10.3390/nu14245381
19. Poudel AN, Zhu S, Cooper N, et al. Impact of Covid-19 on health-related quality of life of patients: a structured review. *PLoS One*. 2021;16:0259164. doi:10.1371/journal.pone.0259164
20. Tan KWA, Koh D. Long COVID-Challenges in diagnosis and managing return-to-work. *J Occup Health*. 2023;65:12401. doi:10.1002/1348-9585.12401
21. Chuang HJ, Lin CW, Hsiao MY, Wang TG, Liang HW. Long COVID and rehabilitation. *J Formos Med Assoc*. 2024;123:61-9.
22. Deng J, Qin C, Lee M, Lee Y, You M, Liu J. Effects of rehabilitation interventions for old adults with long COVID: a systematic review and meta-analysis of randomised controlled trials. *J Glob Health*. 2024;14:05025. doi:10.7189/jogh.14.05025
23. Chatterjee D, Maparu K. Long COVID syndrome: exploring therapies for managing and overcoming persistent symptoms. *Inflammopharmacol*. 2025;33:4097–4113. doi:10.1007/s10787-025-01807-w
24. Gupta S, Liu KR, Sandhu S, Gupta A. *Exercise Interventions for Mitigating the Persistent Side Effects of COVID-19*. Sport Sciences for Health; 2024.
25. Torres G, Gradidge PJ. The quality and pattern of rehabilitation interventions prescribed for post-COVID-19 infection patients: a systematic review and meta-analysis. *Prev Med Rep*. 2023;35:102395. doi:10.1016/j.pmedr.2023.102395
26. Stussman B, Williams A, Snow J, et al. Characterization of post-exertional malaise in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Front Neurol*. 2020;11:1025. doi:10.3389/fneur.2020.01025
27. Sánchez-García JC, Reinoso-Cobo A, Piqueras-Sola B, et al. Long COVID and physical therapy: a systematic review. *Diseases*. 2023;11.
28. Hammami N, Jdidi H, Frih B. COVID-19 pandemic: physical activity as prevention mean. *The Open Sports Sci J*. 2020;13(1):120–122. doi:10.2174/1875399X02013010120
29. Woo AK. Depression and Anxiety in Pain. *Rev Pain*. 2010;4:8-12. doi:10.1177/204946371000400103
30. Surmai M, Duff E. Cognitive behavioural therapy: a strategy to address pandemic-induced anxiety. *J Nurse Pract*. 2022;18:36-9. doi:10.1016/j.nurpra.2021.10.013
31. Russell D, Spence NJ, Chase JD, Schwartz T, Tumminello CM, Bouldin E. Support amid uncertainty: long COVID illness experiences and the role of online communities. *SSM Qual Res Health*. 2022;2:100177. doi:10.1016/j.ssmqr.2022.100177

32. Fong Yan A, Nicholson LL, Ward RE, et al. The effectiveness of dance interventions on psychological and cognitive health outcomes compared with other forms of physical activity: a systematic review with meta-analysis. *Sports Med*. 2024;54(5):1179-205. doi:10.1007/s40279-023-01990-2
33. Sudeck G, Thiel A, Strohacker K. physical activity, subjective well-being and mental health. In: *Éditeurs. Sport and Exercise Psychology: Theory and Application [Internet]*. Cham: Springer International Publishing;2023:649-78. doi:10.1007/978-3-031-03921-8_26
34. Krishna B, Wills M, Sithole N. Long COVID: what is known and what gaps need to be addressed. *Br Med Bull*. 2023;147:6-19. doi:10.1093/bmb/ldad016
35. Ortiz-Ortigosa L, Gálvez-álvarez P, Viñolo-Gil MJ, Rodriguez-Huguet M, Góngora-Rodríguez J, Martín-Valero R. Effectiveness of pulmonary rehabilitation programmes and/or respiratory muscle training in patients with post-COVID conditions: a systematic review. *Respir Res*. 2024;25:248. doi:10.1186/s12931-024-02857-4
36. Izquierdo M, Merchant RA, Morley JE, et al. International Exercise Recommendations in Older Adults (ICFSR): expert consensus guidelines. *j nutr health aging*. 2021;25:824-53.
37. Liu J, Zhai X, Yan W, Liu Q, Liu M, Liang W. Long-term impact of the COVID-19 pandemic on health services utilization in China: a nationwide longitudinal study. *Global Transitions*. 2023;5:21-8. doi:10.1016/j.glt.2023.03.002
38. Guelmami N, Ezzeddine LB, Hatem G, et al. The Ethical Compass: establishing ethical guidelines for research practices in sports medicine and exercise science. *Int J Sport Studies for Health*. 2024;7(2):31-46. doi:10.61838/kman.intjssh.7.2.4
39. Kang H. Sample size determination and power analysis using the G*Power software. *J Educ Eval Health Prof*. 2021;18:17. doi:10.3352/jeehp.2021.18.17
40. Soh SE, Morello R, Ayton D, et al. Measurement properties of the 12-item short form health survey version 2 in Australians with lung cancer: a rasch analysis. *Health Qual Life Outcomes*. 2021;19:157. doi:10.1186/s12955-021-01794-w
41. Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. *ERJ Open Res*. 2017;3.
42. Rishi P, Rishi E, Maitray A, Agarwal A, Nair S, Gopalakrishnan S. Hospital anxiety and depression scale assessment of 100 patients before and after using low vision care: a prospective study in a tertiary eye-care setting. *Indian J Ophthalmol*. 2017;65:1203-8. doi:10.4103/ijo.IJO_436_17
43. Kammin EJ. The 6-minute walk test: indications and guidelines for use in outpatient practices. *J Nurse Pract*. 2022;18:608-10. doi:10.1016/j.nurpra.2022.04.013
44. Ponce MC, Sankari A, Sharma S.Pulmonary Function Tests. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. Available from: http://www.ncbi.nlm.nih.gov/books/NBK482339/. Accessed October 3, 2025.
45. Akoglu H. User's guide to correlation coefficients. *Turk J Emerg Med*. 2018;18:91-3. doi:10.1016/j.tjem.2018.08.001
46. Richardson JTE. Eta squared and partial eta squared as measures of effect size in educational research. *Educational Res Rev*. 2011;6:135-47. doi:10.1016/j.edurev.2010.12.001
47. Divine G, Norton HJ, Hunt R, Dienemann J. Statistical grand rounds: a review of analysis and sample size calculation considerations for Wilcoxon tests. *Anesth Analg*. 2013;117:699-710. doi:10.1213/ANE.0b013e31827f53d7
48. Daynes E, Gerlis C, Chaplin E, Gardiner N, Singh SJ. Early experiences of rehabilitation for individuals post-COVID to improve fatigue, breathlessness exercise capacity and cognition - A cohort study. *Chron Respir Dis*. 2021;18:14799731211015691. doi:10.1177/14799731211015691
49. Gloeckl R, Zwick RH, Fürlinger U, et al. Practical recommendations for exercise training in patients with long COVID with or without post-exertional malaise: a best practice proposal. *Sports Med Open*. 2024;10:47. doi:10.1186/s40798-024-00695-8
50. Mahindru A, Patil P, Agrawal V. Role of physical activity on mental health and well-being: a review. *Cureus*. 2023;15:33475.
51. Mingoti MED, Bertollo AG, Simões JLB, Francisco GR, Bagatini MD, Ignácio ZM. COVID-19, oxidative stress, and neuroinflammation in the depression route. *J Mol Neurosci*. 2022;72:1166-81. doi:10.1007/s12031-022-02004-y
52. Witteveen AB, Young S, Cuijpers P, et al. Remote mental health care interventions during the COVID-19 pandemic: an umbrella review. *Behav Res Ther*. 2022;159:104226. doi:10.1016/j.brat.2022.104226
53. Pahlavani HA. Possible role of exercise therapy on depression: effector neurotransmitters as key players. *Behav Brain Res*. 2024;459:114791. doi:10.1016/j.bbr.2023.114791
54. Bjørlykhaug KI, Karlsson B, Hesook SK, Kleppe LC. Social support and recovery from mental health problems: a scoping review. *Nordic Soc Work Res*. 2022;12:666-97. doi:10.1080/2156857X.2020.1868553
55. Nopp S, Moik F, Klok FA, et al. Outpatient pulmonary rehabilitation in patients with long COVID improves exercise capacity, functional status, dyspnea, fatigue, and quality of life. *Respiration*. 2022;101:593-601. doi:10.1159/000522118
56. Stutz J, Casutt S, Spengler CM. Respiratory muscle endurance training improves exercise performance but does not affect resting blood pressure and sleep in healthy active elderly. *Eur J Appl Physiol*. 2022;122:2515-31. doi:10.1007/s00421-022-05024-z
57. Marini CF, Federici A, Skinner JS, et al. Effect of steady-state aerobic exercise intensity and duration on the relationship between reserves of heart rate and oxygen uptake. *PeerJ*. 2022;10:13190. doi:10.7717/peerj.13190
58. Cravo A, Attar D, Freeman D, Holmes S, Ip L, Singh SJ. The importance of self-management in the context of personalized care in COPD. *Int J Chron Obstruct Pulmon Dis*. 2022;17:231-43. doi:10.2147/COPD.S343108
59. Rezaei S, Matin BK, Karyani AK, et al. Impact of smoking on health-related quality of life: a general population survey in West Iran. *Asian Pac J Cancer Prev*. 2017;18:3179-85. doi:10.22034/APJCP.2017.18.11.3179
60. Trofor AC, Popa DR, Melinte OE, et al. Looking at the Data on Smoking and Post-COVID-19 Syndrome-A. *Literature Rev J Pers Med*. 2024;14.
61. Farrell SF, Edmunds D, Fletcher J, et al. Effectiveness of psychological interventions delivered by physiotherapists in the management of neck pain: a systematic review with meta-analysis. *Pain Rep*. 2023;8:1076. doi:10.1097/PR9.0000000000001076
62. Rando HM, Bennett TD, Byrd JB, et al. Challenges in defining Long COVID: striking differences across literature, electronic health records, and patient-reported information. *medRxiv*. 2021.
63. Colas C, Berre YL, Fanget M, et al. Physical activity in long COVID: a comparative study of exercise rehabilitation benefits in patients with long COVID, coronary artery disease and fibromyalgia. *Int J Environ Res Public Health*. 2023;21:20. doi:10.3390/ijerph21010020
64. Kasiak P, Kowalski T, Klusiewicz A, et al. Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study. *Sci Rep*. 2024;14(1):23133. doi:10.1038/s41598-024-73730-z