Effects of physical training on the quality of life of patients with post-COVID-19 condition

Efeitos do treinamento físico na qualidade de vida de pacientes com síndrome pós-COVID-19

Andreane Daniele Barbosa de Lira [1,2*]
Alexandra Ignes Bruni Tulio [1,2]
Heloísa Rodrigues Alves Bobato [2]
Regina Helena Senff Gomes [2]
Arlete Ana Motter [1]

[1] Universidade Federal do Paraná (UFPR), Programa de Pós-Graduação em Saúde Coletiva, Curitiba, PR, Brazil
[2] Complexo do Hospital de Clínicas, Universidade Federal do Paraná (UFPR) - Empresa Brasileira de Serviços Hospitalares (EBSERH), Curitiba, PR, Brazil

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***Correspondence:** andreane.daniele@gmail.com

Abstract

Introduction: Post-COVID-19 condition has a significant impact on the quality of life (QOL) of the affected individuals. **Objective:** To describe the effects of a pulmonary rehabilitation (PR) program on the health-related quality of life (HRQOL) of patients with post-COVID-19 condition and understand the aspects relevant to their quality of life. **Methods:** This is a quasi-experimental study, using an interrupted time series design, involving adult men and women with a history of hospitalization due to SARS-CoV-2 and post-COVID-19 condition who were referred for PR between February 2021 and December 2022. Participants were assessed pre- and post-PR for clinical information, quality of life (using the Nottingham Health Profile - NHP), overall peripheral muscle strength (dynamometry), and dyspnea during activities of daily living (ADLs) (mMRC scale). **Results:** Thirty-nine individuals participated in the study, 22 (56.4%) of whom were women, with a mean age of 55.8 (± 9.98) years. The most common persistent symptoms were fatigue (64.1%), dyspnea (59%), memory impairment (30.8%), and pain (28.2%). Of the six NHP domains, five showed significant improvement after the intervention. The median total NHP score decreased from 11 points pre-PR to 6 points post-PR ($p < 0.001$). Dynamometry and mMRC scores also exhibited statistically significant improvements after PR. **Conclusion:** Individuals with post-COVID-19 condition experience important impairments in HRQOL, across physical, emotional, social, and sleep-related domains. Pulmonary rehabilitation, through physical training, produced positive effects by improving QOL, increasing overall peripheral muscle strength, and reducing dyspnea during ADLs.

Keywords: Physiotherapy. COVID-19. SARS-CoV-2. Long COVID. Rehabilitation.

Resumo

Introdução: *A síndrome pós-COVID-19 tem impacto significativo na qualidade de vida dos indivíduos acometidos.* ***Objetivo:*** *Descrever os efeitos de um programa de reabilitação pulmonar (RP) sobre a qualidade de vida relacionada à saúde (QVRS) de pacientes com síndrome pós-COVID-19 e compreender os aspectos pertinentes à qualidade de vida destes pacientes.* ***Métodos:*** *Trata-se de um estudo quase-experimental, do tipo série de tempo interrompida, com adultos de ambos os sexos, com histórico de internação pelo SARS-CoV-2 e síndrome pós-COVID-19, encaminhados para RP entre fevereiro/2021 e dezembro/2022. Os participantes foram avaliados quanto às informações clínicas, qualidade de vida (Perfil de Saúde de Nottingham - PSN), força muscular periférica global (dinamometria) e dispneia às atividades de vida diária (escala mMRC) pré e pós-RP.* ***Resultados:*** *Participaram do estudo 39 sujeitos, sendo 22 (56,4%) do sexo feminino, com idade média de 55,8 (+ 9,98) anos. As principais queixas persistentes foram fadiga (64,1%), dispneia (59%), alteração de memória (30,8%) e dor (28,2%). Dos seis domínios do PSN, cinco apresentaram melhora significativa pós-intervenção. A mediana do escore total do PSN foi de 11 pontos no pré para 6 pontos no pós-RP (p < 0,001). Dinamometria e mMRC também apresentaram diferença estatística significativas pós-RP.* ***Conclusão:*** *Indivíduos com síndrome pós-COVID-19 apresentam alterações importantes na QVRS, evidenciadas por alterações físicas, emocionais, sociais e do sono. A RP, por meio do treinamento físico, demonstrou efeitos positivos na melhoria da qualidade de vida e também sobre o ganho de força muscular periférica global, e redução da dispneia às atividades de vida diária.*

Palavras-chave: *Fisioterapia. COVID-19. SARS-CoV-2. COVID longa. Reabilitação.*

Introduction

Following the acute phase of the pandemic, it is now understood that the impact of SARS-CoV-2 infection extends beyond the initial illness. Between 10 and 20% of those who recover from the disease experience symptoms that negatively affect their health and quality of life (QOL), a condition known as post-COVID-19 condition.[1]

Post-COVID-19 condition, also referred to as long COVID, is characterized by a set of symptoms that persist or emerge for the first time after the SARS-CoV-2 infection, and may last for weeks or months after the initial recovery phase.[1-4] What differentiates long COVID from other post-viral syndromes is its considerably higher epidemiolo-gical burden, up to six times more prevalent than similar conditions resulting from other viral infections.[5]

The lingering effects of SARS-CoV-2 infection can impact multiple organ systems, commonly leading to fatigue or muscle weakness, dyspnea, chest pain, sleep and emotional disturbances, arthralgia, and a decline in QOL.[2,6-9] Multiple, potentially overlapping factors are believed to contribute to post-COVID-19 condition. These include persistent SARS-CoV-2 reservoirs in tissues, immune dysregulation, sustained inflammation, tissue dysfunction and damage resulting from excessive inflammation, nonspecific effects of hospitalization, sequelae of critical illness, comorbidity-related complications, and adverse effects of medications.[10-12]

Prolonged symptoms are a significant burden on the quality of life QOL of COVID-19 survivors, and may persist for months following the acute infection.[4,13] Moreover, evidence suggests that post-COVID-19 condition may become a major psychosocial and economic challenge.[14]

It is well established that the repercussions of a disease extend beyond clinical outcomes such as mortality and morbidity, encompassing subjective measures including health-related quality of life (HRQOL). This multidimensional construct includes physical, mental, social, and emotional domains and can be assessed through generic or specific instruments validated for different populations.[15]

In public health research and practice, QOL measures are valid and appropriate indicators of intervention outcomes, incorporating objective and subjective evaluations. These HRQOL data help determine public policies, planning strategies, and therapeutic interventions.[16]

Consequently, investigating HRQOL is crucial for evaluating the impact of diseases, disorders, or impairments in physical, mental, and social domains.[17] Thus, patient-reported QOL is also a significant parameter for identifying individuals with a substantial burden of post-COVID-19 symptoms.[14]

Among multiple treatments, physiotherapy through exercise-based pulmonary rehabilitation (PR) programs is effective in improving functional capacity, dyspnea, and HRQOL, as demonstrated by studies related to other pulmonary diseases.[18,19]

Given the above, the present study aimed to describe the effects of a PR program on the HRQoL of patients with post-COVID-19 condition and understand the aspects relevant to their quality of life.

Methods

This is a quasi-experimental study using an interrupted time series design, and a convenience sample of adults with post-COVID-19 condition referred for PR between February 2021 and December 2022.

The research was conducted at the Physiotherapy Outpatient Clinic of the Hospital de Clínicas Complex at the Federal University of Paraná, following approval by the Research Ethics Committee (CAAE: 47158821. 6.0000.0096, protocol number 4.805.035). All participants who agreed to take part in the study gave their written informed consent.

Inclusion criteria were history of hospitalization with a positive COVID-19 test, age > 18 years, both sexes, not currently engaged in physical activity, and a medical referral for PR. Exclusion criteria included pre-existing motor/functional impairments, severe cardiovascular diseases, cognitive impairments, pregnant and puerperal women, peripheral oxygen saturation < 80% at rest, resting heart rate above the maximum recommended for age, and any limitation and/or contraindication to aerobic training.

For data collection, a standardized evaluation form developed by the researchers, encompassing sociodemographic, anthropometric, and clinical information, was used. Body mass index (BMI) was calculated using weight and height, and individuals with a BMI exceeding 30 kg/m² were classified as obese, and those below as non-obese.[20]

The Nottingham Health Profile (NHP) was used to assess HRQOL. This is a generic QOL assessment instrument comprising 38 items based on the World Health Organization's disability classification, with "yes" or "no" response options. The items are categorized into six domains: energy level (3 items), pain (8 items), emotional reactions (9 items), sleep (5 items), social interaction (5 items), and physical skills (8 items). Each "yes" response is scored as one (1) point, and each "no" response as zero (0), resulting in a maximum score of 38, where higher scores indicate poorer QOL.[21]

Overall peripheral muscle strength was also evaluated using the handgrip strength test, based on the maximum value recorded by dynamometry, a simple yet valid measure of overall muscle strength.[22] Participants were seated with the dominant upper limb flexed at the elbow at a 90° angle, and the forearm close to the body. They were instructed to apply maximum grip force for approximately three seconds using a hydraulic hand dynamometer (Saehan Medical, model SH5001), with a 15-second rest period. Three measurements were obtained, and the highest value was used for analysis.

Dyspnea experienced during ADLs was assessed using the Modified Medical Research Council Dyspnea Scale (mMRC). Participants reported their perceived level of dyspnea by selecting a score ranging from 0 to 4, where 0 = dyspnea only with strenuous exercise; 1 = breathlessness when walking quickly on level ground or up a gentle slope; 2 = walking slower than others the same age due to breathless or stopping for breath when walking at own pace on level ground; 3 = short of breath after walking a few minutes or 90 to 120 meters on level ground; 4 = too breathless to leave the house or breathless when dressing or undressing.[23]

All participants were evaluated before and after the intervention by one of the study's physiotherapists, who had been previously trained in the protocol, and assessed HRQOL (NHP), overall peripheral muscle strength (dynamometry), and dyspnea during ADLs (mMRC).

To determine the appropriate aerobic training load, all participants underwent an incremental lower-limb exercise test on a treadmill or stationary bicycle during the initial assessment. The test began with a 3-minute warm-up at zero incline, to allow participants to establish a comfortable walking or cycling speed. Following the warm-up, the treadmill incline was increased by 1% per minute, while monitoring heart rate, oxygen saturation, and the Borg scale (ranging from 0, indicating no effort to 10, indicating maximal effort) for both dyspnea and lower-limb fatigue. The test was terminated based on the participants' perception of dyspnea or fatigue (Borg scale), pain, or if their heart rate exceeded the predicted maximum. The test (excluding warm-up) lasted between 8 and 12 minutes.

If the test duration fell outside this range, it could be repeated on a subsequent day with adjustments to the initial speed. For participants unable to use the treadmill, the test was administered on a stationary bike, with workload increments measured in watts. For rehabilitation, 80% of the maximum load achieved during the test was prescribed, while maintaining the established speed.[24]

The proposed intervention consisted of eight weeks of PR involving physical training, at a frequency of two to three individual one-hour sessions per week. These sessions were conducted under the direct supervision of a physiotherapist, with continuous monitoring of maximum heart rate, oxygen saturation, and perceived exertion. The PR protocol used in this study is presented in Table 1.

Table 1 - Proposed rehabilitation program

Protocol	Exercises	Time (minutes)
Warmup	Active upper limb exercises, static gait	5
Aerobic training	Treadmill or stationary bicycleat 80% of incremental test load	30
Muscle strengthening	Upper and lower limbs,3 sets of 8 to 12 repetitions	5
Functional training	Balance and gait training, functional exercises	5
Muscle stretching	Global	8
Breathing exercises	Ventilatory patterns, broncheal hygiene (if needed)	5
Guidance	Educational guidance on the diseases, preventive easures and at-home exercises	2
Oxygen supplementation	If peripheral oxygen saturation (SpO_2) < 88%, follow the same incremental test parameters	Time required to adapt SpO_2

Statistical analysis

The collected data were tabulated and analyzed using Jamovi statistical software (version 2.5.0). Results are presented as means with standard deviations, and absolute and relative frequencies, according to the nature of the variable. The Shapiro-Wilk test was used to assess the normality of data distribution. To determine statistical significance, different tests were applied, based on the type of variable. For quantitative variables exhibiting a normal distribution, the parametric paired Student's t-test was used. For quantitative variables lacking a normal distribution or ordinal qualitative variables, the Wilcoxon non-parametric test was applied.

To conduct a multivariate analysis of the effect of time on the NHP score, a linear mixed-effects model was constructed using REML (Restricted Maximum Likelihood Estimation). The dependent variable was the NHP score, and predictor variables were selected based on their theoretical relevance. The model's goodness of fit was assessed using quality metrics such as AIC (Akaike Information Criterion), BIC (Bayesian Information Criterion), R-squared (R^2) and ICC (Intraclass Correlation Coefficient). For all statistical tests, the significance level was set at $p < 0.05$.

Results

During the study period, a total of 71 individuals visited the physiotherapy clinic for PR due to post-COVID-19 condition, 46 of whom met the inclusion criteria and were subsequently recruited. Among the eligible paricipants, seven were lost to follow-up (Figure 1).

The final sample consisted of 39 participants with post-COVID-19 condition, 22 (56.4%) of whom were women, with a mean age of 55.8 years (± 9.98), a mean BMI of 32 kg/m^2 (± 4.52), and mean hospital stay due to COVID-19 of 25.5 days (± 15.9). The primary comorbidities were obesity, present in 27 individuals (69.2%), and hypertension, in 22 (56.4%). The most frequently reported persistent symptoms included fatigue, reported by 25 participants (64.1%), dyspnea by 23 (59%), memory impairment by 12 (30.8%), and pain by 11 (28.2%) Additional epidemiological data for the sample are presented in Table 2.

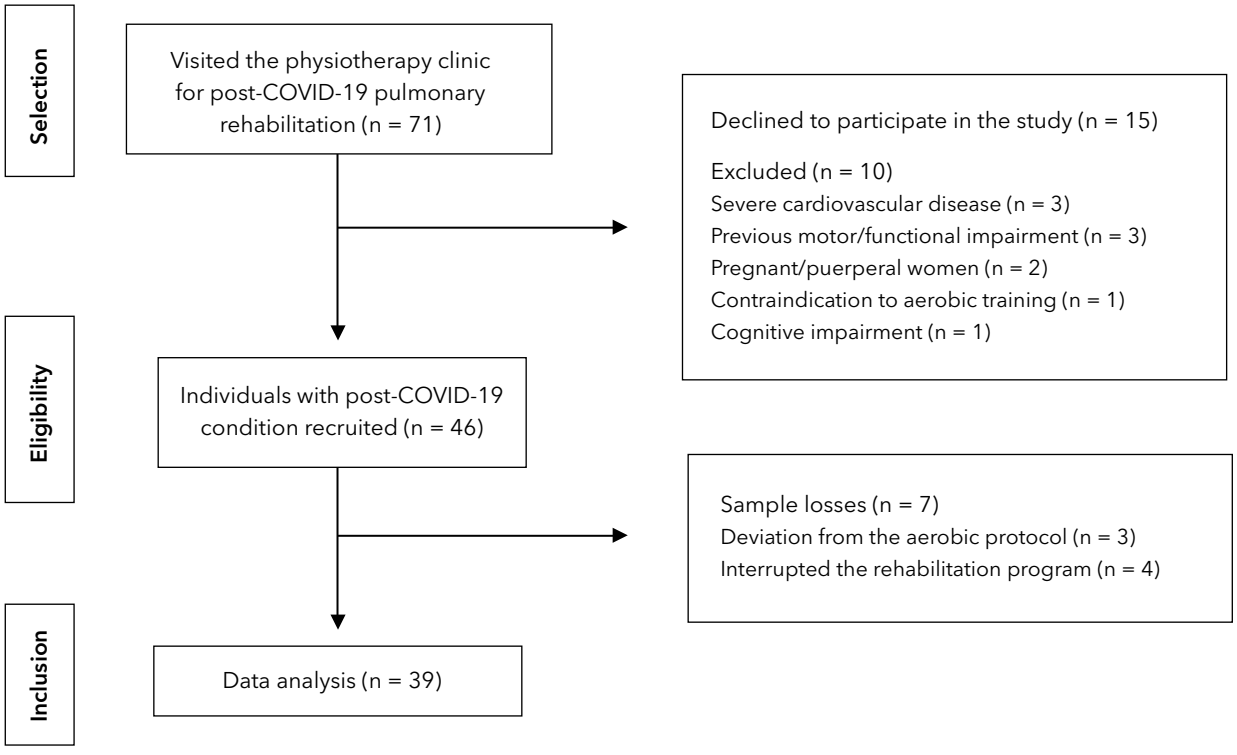

Figure 1 - Flowchart of data collection.

Table 2 - Overall study participant data (n = 39)

Overall Data	n (%)
Women	22 (56.4)
Men	17 (43.6)
Age (years)*	55.80 ± 9.98
Body mass index*	32.00 ± 4.52
Days hospitalized*	25.50 ± 15.90
Days in the intensive care unit*	14.50 ± 16.20
Days on invasive mechanical ventilation*	9.59 ± 12.10
Comorbidities	
Obesity	27 (69.2)
Hypertension	22 (56.4)
Dyslipidemia	9 (23.1)
Diabetes	8 (20.5)
Hypothyroidism	7 (17.9)
Complaints	
Fatigue	25 (64.1)
Dyspnea	23 (59.0)
Memory impairment	12 (30.8)
Pain	11 (28.2)
Others	17 (43.6)

Note: *Data shown as mean and standard deviation.

In the initial QOL assessment, conducted using the NHP, all participants reported a certain level of impairment in some of the items evaluated, with a minimum of 1 and maximum of 30 affirmative responses. Among the 38 items comprising the NHP questionnaire, five exhibited the highest affirmative response frequencies before the intervention, with significant percentages, as follows: Item 26 – "I lose my energy quickly" (energy level domain) was reported by 64.1% of participants; Item 17 – "I have difficulty climbing up and down stairs or steps" (physical abilities domain) by 61.5% of participants; Item 11 – "I have difficulty bending down" (physical abilities domain) by 59%; Item 27 – "I have difficulty standing for long periods (at the kitchen sink or waiting for the bus)" (physical abilities domain) by 59%; and Item 3 – "Things are making me feel discouraged/depressed" (emotional reactions domain) by 51.3%.

Following the intervention protocol, all these items showed improvement, with affirmative response frequencies decreasing to 25.6% for items 26, 17, and 11, 51.3% for item 27 and 10.3% for item 3. For the remaining items, the affirmative response frequencies varied from 0 to 48.7% before and 0 to 35.9% after the intervention.

In regard to HRQOL, with respect to NHP domains, while the "social interaction" domain showed a trend toward improvement, this change was not statistically significant (p = 0.086). However, all the other domains, namely, energy le-vel, pain, emotional reactions, sleep, and physical skills, improved substantially, as shown in Table 3. This posi-tive impact on QOL is also supported by the total NHP score, which decreased from a median of 11 points pre-rehabilitation to 6 points post-rehabilitation (p < 0.001). With respect to global peripheral muscle strength (assessed by dynamometry) and dyspnea during ADLs (assessed by the mMRC scale), which were also investigated in this study, the intervention improved muscle strength and reduced dyspnea (Table 3).

Table 3 - Measures of the variables before and after the pulmonary rehabilitation protocol (PRP)

Variables	Pre-PRP	Post-PRP	p-value*
Quality of life			
Energy level domain	1 [0.0 – 1.0]	0 [0.0 – 1.0]	0.001
Pain domain	2 [1.0 – 5.0]	1 [0.0 – 3.0]	0.014
Emotional reaction domain	4 [0.0 – 4.0]	1 [0.0 – 2.0]	< 0.001
Sleep domain	1 [0.5 – 3.5]	1 [0.0 – 2.0]	0.001
Social interaction domain	0 [0.0 – 2.0]	0 [0.0 – 1.0]	0.086
Physical skills domain	3 [2.0 – 4.0]	1 [0.0 – 2.0]	< 0.001
Total NHP score	11 [7.0 – 16.5]	6 [3.0 – 11.0]	< 0.001
Overall peripheral muscle strength			
Dynamometry	28 [22.0 – 32.0]	30 [24.0 – 35.0]	< 0.001
Dyspnea during ADLs			
mMRC	2 [1.0 – 3.0]	1 [0.0 – 1.0]	< 0.001

Note: NHP = Nottingham Health Profile; ADLs = activities of daily living; mMRC = Modified Medical Research Council Dyspnea Scale.

Regression analysis using a mixed linear model confirmed that the difference between pre- and post-intervention NHP scores had an estimated effect of -4.94, with a standard error of 0.82 and 95% confidence interval ranging from -6.57 to -3.32. This effect was statistically significant (t = -5.96; p < 0.001), indicating an improvement in QOL, independent of other variables.

The model also revelead that age had a significant negative effect (t = -2.48; p = 0.019), with an estimate of -0.25 and a standard error of 0.10, suggesting that older age is associated with a smaller change in the total NHP score. The significant interaction between the difference in post- and pre-intervention scores and age (t = 2.25; p = 0.03) indicates that the change in NHP scores resulting from the rehabilitation program varied according to age. The other variables included in the mixed linear model showed no significant effects (Table 4). The model demonstrated a good overall fit, evidenced by the high R^2 value (coefficient of determination = 0.75), demonstrating that 75% of the variability in the NHP score was explained by the model, and moderate data reliability, as indicated by the ICC of 0.58.

Discussion

The demographic profile of the study sample indicated that 56.4% were women. This suggests a potential tendency for women to require referral for pulmonary rehabilitation due to post-COVID-19 condition. Several authors have reported a higher risk for long-term symptoms, such as persistent dyspnea and fatigue, in women.[25] It is well-established that post-COVID-19 condition can manifest in patients who experienced both severe and mild or moderate forms of the disease. However, evidence suggests that 30% of hospitalized patients with SARS-CoV-2 develop the chronic form.[26] Hospitalization for COVID-19 was an inclusion criterion for this study, with an average stay of 25.5 days, corroborating literature findings.

Table 4 - Multivariate analysis of the effect of time on the Nottingham Health Profile (NHP) score using a mixed linear model regression

Variables	Estimate (β)	SE	CI (95%)	df	t	p-value
Intercept	10.05	0.89	8.29/11.81	30	11.19	< 0.010
Group 1 (NHP post-PR/pre-PR)	-4.94	0.82	-6.57/-3.32	37	-5.96	< 0.001
Sex (Male/Female)	-2.52	2.41	-7.26/2.22	30	-1.04	0.306
Age	-0.25	0.10	-0.44/-0.05	30	-2.48	0.019
IMV duration (days)	-8.68	0.06	-0.13/0.13	30	-0.01	0.990
Obesity (Yes/No)	-3.32	2.15	-7.54/0.88	30	-1.54	0.132
mMRC pre-PR	0.87	1.19	-1.46/3.21	30	0.73	0.467
mMRC post-PR	1.37	1.34	-1.26/4.01	30	1.01	0.316
Dynamometry pre-PR	-0.21	0.32	-0.86/0.42	30	-0.66	0.510
Dynamometry post-PR	0.05	0.33	-0.60/0.71	30	0.16	0,872
Group 1 (NHP post-PR/pre-PR) *Age	0.18	0.08	0.02/0.35	37	2.25	0.030

Note: Data presented as coefficient (β) and confidence interval (CI). SE = standard error; df = degrees of freedom; t = t-statistic; PR = pulmonary rehabilitation; IMV = invasive mechanical ventilation; mMRC = modified Medical Research Council dyspnea scale.

With respect to the incidence of comorbidities, the high prevalence of obesity, present in 69.2% of the subjects in this analysis, warrants attention. Thus, it can be inferred that obese patients are more susceptible to the persistent symptoms of COVID-19.

In Latin America, studies have shown that individuals with obesity infected with SARS-CoV-2 are 113% more likely to require hospital care, 74% more likely to need intensive care, and 48% more likely to die when compared to normal weight individuals.[27]

Among patients with post-COVID-19 condition, long-term symptoms vary. In this sample, the most frequent complaints were fatigue, dyspnea, memory impairment, and pain. Similarly, a study conducted 12 months after the viral infection also concluded that mainly fatigue and memory impairment persisted for more than one year in these patients.[28]

All participants in this study reported some level of QOL decline, as evidenced by at least one positive response on the NHP. The persistent symptoms reported (fatigue, dyspnea, memory impairment, pain) alone could account for this alteration in HRQOL. Furthermore, the duration of hospitalization, and the potential post-traumatic stress and anxiety arising from post-illness uncertainties, may also have contributed to this impairment. These assumptions are also supported by existing literature on the topic.[29]

The high pre-intervention frequencies of reported difficulties in performing simple daily tasks such as climbing up and down stairs, bending down, standing for extended periods, and feelings of low energy and discouragement, reinforce the need and responsibility of healthcare professionals to provide comprehensive and well-planned therapy for these individuals, considering physical, emotional, and social aspects. Authors report that integrative care is essential to address the multisystemic needs of this population.[30]

The data presented are consistent with other scientific reports on impaired QOL due to post-COVID-19 condition, where difficulties in performing daily activities, such as washing and dressing, and an inability to maintain routine activities, were observed, contributing to feelings of frustration and guilt and generating a high level of stress.[29] Assessment of the clinical variables measured through the research protocols demonstrated that the eight-week PR program using physical training improved HRQOL.

In this context, the "energy level," "pain," "emotional reactions," "sleep," and "physical skills domains," exhibiting significantly lower scores after the intervention, demonstrate that participants showed improvements in all these categories, which is also confirmed by the reduction in total NHP score. This is a significant finding that, in conjunction with other studies, underscores the

impact of post-COVID-19 condition on physical and emotional function, participation in society, and, consequently, QOL.[31] Pulmonary rehabilitation can be an important strategy for healthcare management in this population. Similarly, the other clinical variables studied also benefited from the intervention, with improvements in peripheral muscle strength and a reduction in dyspnea during ADLs in patients with post-COVID-19 condition.

The findings presented above are consistent with other similar studies, where exercise programs based on PR principles improved the QOL and functional capacity of patients following SARS-CoV-2 infection.[32,33]

The indices suggesting that the change in NHP scores resulting from the rehabilitation program varied according to age, indicating that older age was associated with a smaller change in the total NHP score, could be explained by the aerobic nature of the program. Younger individuals may have experienced more significant benefits and, consequently, a greater effect of time on the score of the assessed instrument.

Overall, this study was relevant because it demonstrated the effects of PR on post-COVID-19 condition, particularly on HRQOL, thereby contributing to the understanding of the therapeutic management of this persistent condition. Despite important results, the quasi-experimental nature of the study introduces some limitations, such as the absence of sample size calculation and a control group. The subsequent significant decrease in the number of patients referred for post-COVID-19 pulmonary rehabilitation following the vaccination campaign, limited the sample size. That being said, the information presented should be critically considered, particularly in view of the small sample size.

Conclusion

Individuals with post-COVID-19 condition experience significant alterations in health-related quality of life, as evidenced by physical and emotional changes. Implementation of a pulmonary rehabilitation protocol, using physical training, demonstrated positive effects in improving this aspect. The protocol also yielded postive outcomes in enhancing overall peripheral muscle strength and reducing dyspnea during activities of daily living. These findings emphasize the importance of pulmonary rehabilitation as an effective strategy for the recovery of patients with post-COVID-19 condition, contributing to restoring functionality and promoting overall well-being.

Authors' contributions

All the authors contributed to the study's conception, design, data analysis, and interpretation. ADBL and AIBT wrote and revised the manuscript, while HRAB, RHSG, and AAM critically reviewed its content. All the authors approved the final version.

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