Effectiveness of Functional or Aerobic Exercise Combined With Breathing Techniques in Telerehabilitation for Patients With Long COVID: A Randomized Controlled Trial

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Objective. The aim of this study was to compare the short-term clinical effects of 2

telerehabilitation programs, functional versus aerobic exercises (AEs), both combined with breathing techniques, regarding the improvement of long coronavirus disease 2019 (COVID-19) symptoms.

Methods. A randomized controlled trial was conducted. The participants were assigned randomly to either the functional exercise (FE) group or AE group, both including breathing techniques. The interventions lasted for 8 weeks with 3 sessions per week, and they were conducted through the Fisiotrack mobile phone application. Assessments were performed at baseline and after treatment, including testing fatigue (Fatigue Assessment Scale), dyspnea (London Chest Activity of Daily Living Scale), functional performance (30 Seconds Standing Test), perceived stress (Perceived Stress Scale), anxiety and depression (Hospital Anxiety and Depression Questionnaire), and quality of life (European Quality of Life Scale). The perceived change after treatment (Patient Global Impression of Change Scale), the usability of the application (System Usability Scale), and the adherence to treatment were also examined after treatment.

Results. In total, 43 participants (FE group, $n = 21$; AE group, $n = 22$; mean age = 42.4 [SD = 6.5] years) completed the study. In the intragroup comparison, the FE group showed improved fatigue (−6.7 points; 95% CI = −11.9 to −1.3), functional capacity (2.6 repetitions; 95% CI = 0.3 to 4.9), and perceived stress (−4.9 points; 95% CI = −9.1 to 0.8), while the AE group showed improved perceived stress (−6.2 points; 95% CI = −10.3 to −2.1). No significant differences in the intergroup effect were identified for the studied variables. Significant differences were observed in the Patient Global Impression of Change Scale in favor of the FE group compared to the AE group, and quality of life reached the minimal clinically important difference for both groups. The ease of use of the telerehabilitation tool was rated excellent in both groups.

Conclusions. Both telerehabilitation exercise modalities are effective at improving stress symptoms and quality of life in patients with long COVID-19. For improving fatigue and functional performance, FE shows more promising results.

Impact. FE or AE may be recommended depending on patients' symptoms, and both may improve quality of life and stress symptoms in patients with long COVID-19. Telerehabilitation may be an optimal intervention modality for the prescription of physical exercise in patients with long COVID-19.

Key words: Exercise; Fatigue; Functional Status; Long COVID; Telerehabilitation

Introduction

Coronavirus disease 2019 (COVID-19) has infected more than 760 million people and resulted in more than 6.9 million deaths worldwide.[1] Among the possible sequelae of the virus, a disorder called long COVID-19 has been shown to affect about 10% of those infected, mostly adult women without previous comorbidities.[2]

Long COVID-19 corresponds to a multisystemic syndrome following the acute period of the disease, in which the person maintains persistent symptoms such as fatigue, dyspnea, cough, memory loss, muscle, and joint pain, among others.[3,4] Breathing techniques have been suggested as a therapeutic option for patients with COVID-19,[5] and they have been included in physical therapist programs for long COVID-19.[6] Moreover, these programs have included aerobic exercises (AEs), or large muscle groups strengthening exercises, and have shown benefits regarding dyspnea, exercise capacity, some pulmonary function variables, and quality of life.[7–10]

Recent studies have shown how programs that combine both aerobic and strengthening exercises can improve the functional capacity of patients with long COVID-19.[6,11] However, there is still no consensus on which of these strategies is more effective at reducing symptoms of patients with long COVID-19. In fact, research focused on other cardiorespiratory health conditions has also shown controversial evidence as to the type of exercise that provides the most benefit. In people with coronary artery disease, a meta-analysis concluded that progressive resistance training produces an increase in overall strength and improved aerobic capacity to a similar degree as aerobic training.[12–14] In patients with chronic obstructive pulmonary disease, low-intensity strength training has been demonstrated to have similar effects on functional capacity to aerobic training[13] and short-term improvements in muscle strength gain, compared to no intervention or AE.[14]

On the other hand, due to the pandemic and the need to reduce the overall geographical mobility of the population, different telerehabilitation strategies have been promoted in physical therapy.[15] Although this modality of work has some limitations such as the need for basic digital knowledge and internet access, difficulty performing a physical examination, and the scarcity of therapeutic material, it has proven to be a safe and effective strategy in the treatment of conditions similar to COVID-19 with comparable results to face-to-face rehabilitation.[16,17] Mobile apps, in particular, have been shown to reduce the burden on hospitals, provide access to information, and track possible symptoms and the mental health state of individuals.[18] Moreover, these new strategies have been proven to be a safe and low-cost alternative to face-to-face care, as well as being effective when treating similar populations and COVID-19 conditions.[19,20]

Considering long COVID-19 is a relatively new condition, and the available literature is still scarce, determining which exercise modality is more effective in the treatment of persistent symptoms will further optimize recovery times and the resources associated with its treatment. We hypothesized that strengthening exercises such as functional exercises (FEs) would be more effective than aerobic ones, both combined with breathing techniques and applied through telerehabilitation, related to the main symptoms of long COVID-19. The main aim of this study was therefore to compare the short-term clinical effects of 2 telerehabilitation programs, FEs versus AEs, both combined with breathing techniques, on the improvement of long COVID-19 symptoms. A secondary aim was to assess the changes in quality of life and the perception of change after treatment, as well as the usability of the telerehabilitation application.

Methods

Study Design

A single-blind randomized controlled trial was conducted from November 2021 to May 2022, focused on patients with long COVID-19. The participants were randomly allocated into a telerehabilitation 8-week treatment which included breathing techniques and either FEs, which consisted of a strengthening FE protocol, or AE, which included a progressive walking protocol. Assessments were carried out at baseline (T1) and immediately after the intervention (T2).

All participants gave written informed consent, and all procedures were performed in accordance with the ethical standards of the Declaration of Helsinki.[21] The study was approved by the Ethics Committee of the University of Valencia (ID: 15737788). The data were collected at the University of Valencia. This trial is reported to be in accordance with the Consolidated Standards of Reporting Trials guidelines,[22] and the intervention was documented in accordance with the Template for Intervention Description and Replication checklist.[23] The study protocol was registered prospectively on ClinicalTrials.gov (NCT04996212).

Participants

The participants were recruited by contacting the national association of long COVID-19 “LongCovid ACTS (Autonomous Communities Together Spain)” and the regional association “Covid Persistente Comunidad Valenciana.” They were also contacted through dissemination using the official social networks of the University of Valencia and the abovementioned associations.

The inclusion criteria were as follows: age between 20 and 60 years old, having a diagnosis of

COVID-19 confirmed by polymerase chain reaction or an antigen test, the presence of at least 1 of certain persistent symptoms (fatigue, dyspnea, or functional limitation for at least 6 weeks after infection),[3] and having a device with internet access (eg, smartphone, computer, or tablet). The exclusion criteria were as follows: having developed severe disease due to COVID-19 (ie, history of hospitalization, history of severe pneumonia, or pulmonary thromboembolism), diagnosis of another concomitant acute or chronic pulmonary or cardiac pathology, and the presence of more severe symptoms requiring monitoring by clinical staff (ie, desaturation on exertion, instability, or hemodynamic instability).

Sample Size Estimation

Sample size estimation was performed using G*Power (version 3.1; Universität Düsseldorf, Düsseldorf, Germany). Considering that a 4-point difference in the Fatigue Assessment Scale is considered to be a minimal clinically important difference (MCID)[24] and that a previous prospective study found such differences when applying a rehabilitation program in patients after COVID-19,[25] a long effect size ($d = 0.879$) was estimated to calculate the sample size. Then, considering a statistical power of 80% and a significance level of 5%, it was determined that 17 patients per group were needed. The sample size was increased by an additional 15% for possible losses, and the resulting sample size was 20 individuals per group.

Randomization and Masking

Randomization was carried out by an external investigator who was not involved in the assessment or treatment of participants using a randomized sequence using a computer program (https://www.randomizer.org) and a 1:1 ratio. The patients were consecutively assigned to each group as they enrolled in the study. The assessing physical therapists were unaware of the treatment allocation. Due to the nature of the intervention, it was not possible to mask the participants.

Interventions

All interventions were conducted through the Fisiotrack mobile phone application (https://fisiotrack.com/), which allows for the determination of the days of treatment as well as the specific exercises to be performed and dosage and provides audiovisual support material to facilitate the correct execution (Fig. 1). Prior to starting the intervention, the participants were contacted through a personalized video call via Zoom (Zoom Video Communications, Inc, San Jose, CA, USA) by a physical therapist who did not participate in the assessments, to instruct them in the

installation and use of the application.

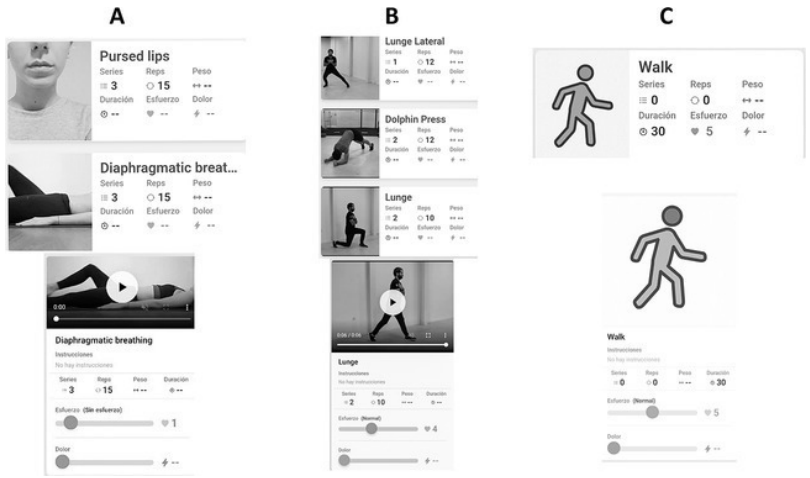

Figure 1 Fisiotrack application audiovisual support material for breathing techniques (A), functional exercise (B), and aerobic exercise (C). Dolor = pain; duración = duration; esfuerzo = effort.

In the same session, the participants in both treatment groups received an educational session to instruct them on how to perform the breathing techniques (diaphragmatic and pursed-lip breathing),[5] which they should do 5 times per week (3 sets, 15 repetitions). This was also controlled by the application.

The duration of each treatment (functional or aerobic) was 8 weeks with a frequency of 3 alternate days/week for about 40 minutes per session (Supplementary Table S1).

FE

FE consisted of a low-intensity strengthening exercise protocol for large muscle groups and included the following exercises[26]: body-weight squat (2 or 3 sets; 10 repetitions), side squat (2 or 3 sets; 10 repetitions), hip thrust (2 or 3 sets; 10 repetitions), front plank (30 seconds), chest press (2 or 3 sets; 10 repetitions), and rowing (2 or 3 sets; 10 repetitions). The exercises were adapted so that each participant could perform them at home, involving their body weight or low weights with readily available items such as water bottles. The participants were also instructed to maintain 1 minute of rest between the sets and between the exercises. The patients were also required to perform a routine of 4 to 6 exercises per sessions increasing in difficulty every 2 weeks

(25 minutes at week 1 up to 40 minutes at week 8), although the fatigue and dyspnea perceived in each exercise could vary the recovery times between the series of exercises.

AE

The patients performed a progressive low-intensity walking protocol,[27] with weekly load adjustments, ranging from 25 to 45 minutes (25 minutes at week 1 up to 45 minutes at week 8). The instruction for the participants was to maintain a walking pace that allowed them to maintain a fluid conversation in order to work at a low exercise intensity.

Both groups were instructed in relation to the intensity of the training which was established using the Talk Test, as it is considered to be a valid and safe test for prescribing exercise.[28] Also, this was used along with the modified Borg Rating of Perceived Exertion, which is a reliable and validated scale for monitoring and guiding exercise intensity by rating the level of exertion during exercise.[29] After explaining the scale in detail for the patients, we asked them to keep the exertion rating level at 4 on the Borg Rating of Perceived Exertion, which suggests that the patient is exercising at a light exercise level. Implementing a low exercise intensity for the peripheral muscles has previously shown high tolerance and simplicity, and improvements have been achieved in the symptoms of people with respiratory impairments.[30]

For both groups, the criteria for stopping the exercise were explained according to the recommendations of the American Thoracic Society and the American College of Chest Physicians: chest pain; headache; sudden weakness; dizziness or lightheadedness; pain in the shoulder, jaw, and/or left arm; disproportionate dyspnea (in relation to exertion); excessive sweating; and/or blurred vision.[31] Moreover, the participants had the choice of contacting the physical therapist if they had any doubts concerning the treatment. The physical therapists responsible for monitoring the training programs had more than 5 years of experience in the field of respiratory physical therapy and therapeutic exercise.

Outcome Measures

The patients were assessed remotely through a structured video call interview conducted by expert physical therapists (A.A.-G., F.M.M.-A., D.H.-G., and C.F.-R.). At T1, demographic and clinical characteristics such as age, sex, educational level, and number of months since infection were recorded. At T2, the variables related to perceived changes and the usability of the application were added.

Primary Outcome

Fatigue

Fatigue was assessed using the Fatigue Assessment Scale, Spanish version,[32] which comprises 10 items, including both physical and mental fatigue. Each item was scored on a scale from 1 ("never") to 5 ("always"). A score of 10 to 21 indicates no fatigue, and a score of 22 to 50 means indicates fatigue, with a higher score indicating a higher level of fatigue. The MCID has a 4-point difference.[24] This instrument has been shown to be valid and reliable for the assessment of fatigue.[33]

Secondary Outcomes

Dyspnea

The Spanish version of the London Chest Activity of Daily Living Scale (LCADL) was used. It assesses the degree of limitation in the activities of daily living (ADL) due to dyspnea using 15 items that consider self-care, household tasks, and physical and leisure activities. Each item was scored from 0 to 5, with 75 being the maximum. A higher score indicates a greater degree of limitation in ADL due to dyspnea. Both LCADL (0–75) and LCADL (percentage) were used for the analysis. To obtain the LCADL (percentage), items with a score of 0 were disregarded, and the new score was calculated according to the proportion of the total score. The MCIDs for this questionnaire were −3 points and − 4 points for LCADL (0–75) and LCADL (percentage), respectively.[34] This questionnaire has been validated and shown to be reliable.[35]

Functional Performance

The 30 Seconds Standing Test (30s-STS) was used. This test has proven to be useful for assessing lower limb strength. The 30s-STS has also been proven to be a reliable and valid test for remote application.[36] The participants performed the 30s-STS test at home under the supervision of a physical therapist. Each participant was asked to use a chair with a backrest and no armrests which was placed with the back against the wall. The instruction was to sit with their back straight, feet flat on the floor**,** and arms crossed over their chest. Each participant was encouraged to get completely up from the chair (knees straight and trunk upright) and to sit back down as many times as possible within 30 seconds.[37] A clinically important improvement of 2 repetitions has been previously described.[38]

Perceived Stress

Perceived stress was assessed using the self-report questionnaire Perceived Stress Scale, Spanish version, which has been validated. The Perceived Stress Scale consists of 14 items related to the respondent's levels of stress during the last month, assessed using a 5-point response system (0 = never, 1 = hardly ever, 2 = occasionally, 3 = often, and 4 = very often). Scores ranging from 0 to 13 are considered low stress, scores of 14 to 26 correspond to moderate stress, and scores of 27 to 40 correspond to high perceived stress.[39]

Anxiety and Depression

The Hospital Anxiety and Depression Questionnaire was used. This instrument consists of 2 subscales, anxiety and depression**,** with 7 items each (range of 0–21 points). A higher score indicates a higher level of anxiety or depression symptoms. A score of 11 or more on each subscale suggests a probable case of anxiety or depression,[40] and the MCID is 1.6.[41]

Quality of Life

Quality of life was assessed using the European Quality of Life Scale. It consists of 5 questions to evaluate the following dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 response categories: no problems, some problems, moderate problems, severe problems, and "unable to."[42] The responses were combined, as described above, to produce an index that was translated into a range of values using an algorithm that varies according to the country of the population. For European populations, the score ranges from −0.208 (worst possible health) to 1.000 (best possible health), so that the higher the score, the better the perception of health status. The patients is 0.051 (0.037–0.063).[42]

Perception of Change after Treatment

Perception of change after treatment was measured using the Patient Global Impression of Change Scale. In the first section, each participant qualitatively indicated perceived changes since before the treatment using a scale that ranged from "very much improved" to "very much worse." It also involved a quantitative visual analog scale that classified the improvement from 0 to 10, where 0 is "I feel much better" and 10 is "I feel much worse."[43] Lower values therefore indicate a greater perception of improvement.[44]

Usability of the Fisiotrack Mobile Application

Usability of the Fisiotrack mobile application was determined with the System Usability Scale, which measures the degree of user satisfaction with the tool through 10 items using a 5-point Likert-type scale. The total score of the tool ranges from 12.5 to 100 points. Scores above 68 indicate good usability, and scores above 80 indicate excellent usability.[45,46]

Adherence to Treatment

Adherence to treatment was assessed by recording the percentage of adherence to each exercise session and was self-reported by the participants through the application.

Statistical Analysis

The normality of the data was checked using the Shapiro–Wilk test. The comparison of baseline characteristics between the 2 groups was then performed using the χ^2 test for categorical variables, the Student *t*-test was done for normally distributed continuous variables, and the Mann–Whitney *U* test was done for any nonparametric variables. The comparison between groups for the variables with a follow-up over time (fatigue, dyspnea, functional capacity, depressive symptoms, perceived stress anxiety symptoms, and quality of life,) was performed using 2-way mixed analysis of variance. The comparison between the groups for the variables with a single measurement time (usability, adherence, and perception of change) was performed using either the Student *t*-test or the Mann–Whitney *U* test, depending on the distribution of the data. A per-protocol analysis was performed inclusive of the participants who completed the treatment plan. Statistical significance was set at $P < .05$. All statistical analyses were performed using SPSS version 22.0 (IBM Corp, Armonk, NY, USA).

Results

Participants

Of the 54 prospective participants, 48 were eligible, agreed to participate, and were randomly assigned to a group. Finally, 43 completed the study (FE group, $n = 21$; AE group, $n = 22$). Figure 2 shows the process of participant recruitment and dropouts. No participants experienced adverse effects.

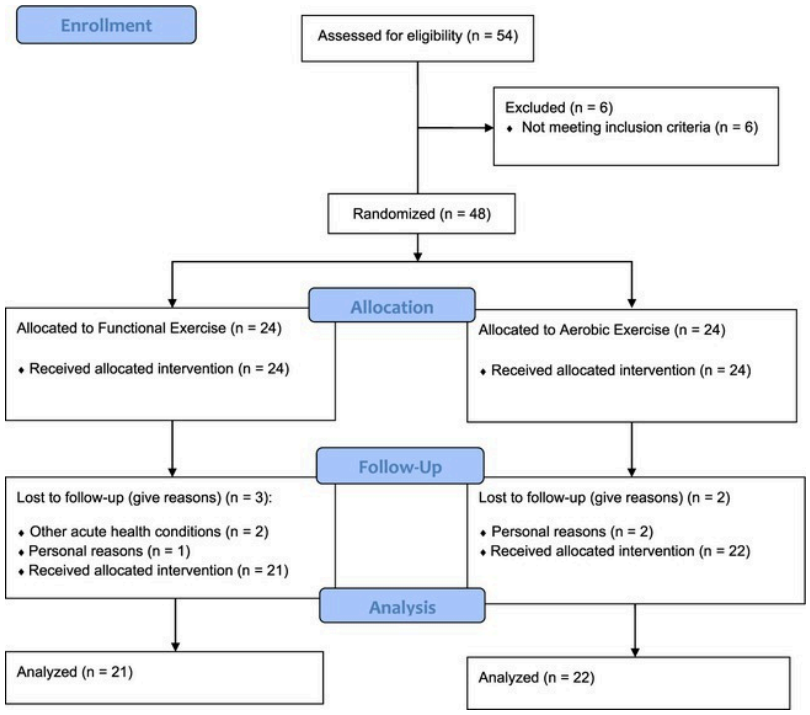

Figure 2 Flowchart according to the CONSORT statement for the reporting of randomized trials.[22]

Therefore, 43 participants were considered for the analysis of this study, with a mean age of 42.4 (SD = 6.5) years, mostly consisting of women (n = 34, 79.1%). Globally, 90.7% had a secondary or higher education level, and an average of 17.4 months had passed since infection. Participants from both groups had a considerable level of fatigue, dyspnea affected their ADL, and they did not perceive themselves as having a high level of quality of life. All data for the demographic and clinical variables and primary and secondary outcome scores at baseline for both groups are shown in Table 1. No significant differences were found when both groups were compared at baseline using these variables.

Table 1 Baseline Comparison Between Groups[a]

Variable	AE Group ($n = 22$)	FE Group ($n = 21$)	*P*
Age, y, mean (SD)	43.8 (5.6)	40.9 (7.1)	.136
Women, no. (%)	17 (77.3)	17 (81)	.532
Educational level, no. (%)			.321
Primary	3 (13.6)	1 (4.8)	
Secondary or higher	19 (86.4)	20 (95.2)	
Time after infection, mo, mean (SD)	17.5 (6.6)	15.8 (8.3)	.463
FAS (10–50), mean (SD)	35.2 (7.4)	32.1 (8.6)	.207
LCADL (0–75), median (IQR)	25 (17.3)	23 (15.5)	.149
LCADL (%), median (IQR)	33.3 (23)	30.7 (20.7)	.149
30s-STS (repetitions), mean (SD)	11.2 (2.4)	12.8 (3.5)	.095
PSS (0–40), mean (SD)	31.0 (4.2)	28.1 (5.7)	.068
HADS-A, mean (SD)	8.1 (4.1)	7.0 (3.5)	.359
HADS-D, mean (SD)	8.1 (4.2)	6.2 (3.5)	.125
EQ-5D-5L (0–1), mean (SD)	0.64 (0.2)	0.69 (0.1)	.650

[a]30s-STS = 30 Seconds Standing Test; AE = aerobic exercise; EQ-5D-5L = European Quality of Life Scale; FAS = Fatigue Assessment Scale; FE = functional exercise; HADS-A = Hospital Anxiety and Depression Scale anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale depression subscale; IQR = interquartile range; LCADL = London Chest Activity of Daily Living Scale; PSS = Perceived Stress Scale.

Table 2 shows the statistical values, significant differences, and minimal clinically important changes of the variables between and within groups. No statistical differences were found between the groups.

Table 2 Pre- and Post-telerehabilitation Differences[a]

Variable	AE Group ($n = 22$)			FE Group ($n = 21$)			Intergroup Difference		
	After Telerehabilitation[b]	Mean Difference (95% CI)	*P*	After Telerehabilitation[b]	Mean Difference (95% CI)	*P*	$F_{(1,82)}$	*P*	η^2 *P*
FAS (10–50)	30.1 (1.9)[c]	−5.1 (−10.3 to 0.1)	.055	25.4 (1.9)[c]	−6.7 (−11.9 to −1.3)	.015[d]	0.177	.675	.002
LCADL (0–75)	24.2 (2.0)	−5.6 (−11.4 to 0.2)	.056	22.4 (2.1)	−0.9 (−4.9 to 6.7)	.762	1.292	.259	.016
LCADL (%)	32.3 (2.7)	−7.5 (−15.2 to 0.2)	.056	29.8 (2.7)	−1.2 (−9.1 to 6.7)	.763	1.292	.259	.016
30s-STS (repetitions)	12.5 (0.8)	1.2 (−1.0 to 3.4)	.276	15.4 (0.8)	2.6 (0.3 to 4.9)	.025[d]	0.757	.387	.009
PSS (0–40)	24.9 (1.5)	−6.2 (−10.3 to −2.1)	.004[d]	23.2 (1.5)	−4.9 (−9.1 to 0.8)	.021[d]	0.174	.678	.002
HADS-D (0–21)	6.0 (0.9)[c]	−2.0 (−4.8 to 0.4)	.098	5.8 (0.9)	−0.5 (−3.0 to 2.0)	.704	0.807	.372	.010
HADS-A (0–21)	7.1 (0.8)	−1.0 (−3.1 to 1.2)	.437	6.9 (0.8)	−0.1 (−2.3 to 2.1)	.933	0.303	.584	.004
EQ-5D-5L (0–1)	0.72 (0.1)[c]	0.1 (−0.1 to 0.2)	.306	0.78 (0.1)[c]	0.1 (−0.2 to 0.2)	.145	0.175	.675	.002

[a]30s-STS = 30 Seconds Standing Test; AE = aerobic exercise; EQ-5D-5L = European Quality of Life Scale; FAS = Fatigue Assessment Scale; FE = functional exercise; HADS-A = Hospital Anxiety and Depression Scale anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale depression subscale; LCADL = London Chest Activity of Daily Living Scale; PSS = Perceived Stress Scale.

[b]Reported as mean (SD).

[c]Meets criteria for minimal clinically important difference.
[d]Statistically significant difference ($P < .05$).

Primary and Secondary Outcomes

There were statistically significant differences within the FE group for fatigue, functional performance**,** and perceived stress. Moreover, fatigue and quality of life exhibited clinically significant improvements after treatment within the FE group (−4 and − 0.051, respectively). Regarding the AE group, there were significant differences within the group for perceived stress and clinically significant improvements for fatigue, quality of life, and depression symptoms (−4, −0.051, and − 1.6, respectively) after treatment.

Regarding the global perception of change reported by the patients using the quantitative question of the Patient Global Impression of Change Scale, statistically significant differences were found in favor of the FE group compared to the AE group ($P < .05$) (Tab. 3). Significant differences were also observed in the categorical Patient Global Impression of Change Scale in favor of the FE group ($\chi^2 = 11.48$; $P = .019$).

Table 3 Comparison of Groups for Usability, Adherence, and Perception of Change[a]

Variable	AE Group ($n = 22$)	FE Group ($n = 21$)	*P*
PGIC Scale (0–10), mean (SD)	4.0 (1.1)	3.1 (1.5)	.042[b]
PGIC Scale category, no. (%)			.019[b]
Very much improved	0 (0)	2 (9.5)	
Much improved	3 (13.6)	11 (52.4)	
Minimally improved	11 (50)	3 (14.3)	
No change	5 (22.7)	3 (14.3)	
Worse	3 (13.6)	2 (9.5)	
Much worse	0 (0)	0 (0)	
Very much worse	0 (0)	0 (0)	

Variable	AE Group ($n = 22$)	FE Group ($n = 21$)	*P*
SUS (0–100), median (minimum to maximum)	90 (50–100)	86 (72.5–92.5)	.403
Adherence (%), median (minimum to maximum)	89 (44–100)	96 (78–100)	.118

[a]AE = aerobic exercise; FE = functional exercise; PGIC = Patient Global Impression of Change; SUS = System Usability Scale.
[b]Statistically significant difference ($P < .05$).

In relation to the usability of the Fisiotrack application, it was determined to be a highly valued tool by the participants of both groups (86 points for the FE group and 90 points for the AE group), registering above the cutoff score of 68 points, which determines the usability of the instrument. Finally, the percentages of compliance with the treatment plan were 96% for the FE group and 89% for the AE group; thus, both of them showed high values of adherence (Tab. 3).

Discussion

The present randomized controlled trial involving patients with long COVID-19 showed that in a multicomponent telerehabilitation program when breathing techniques were combined with FEs, fatigue, functional capacity, and perceived stress improved in the short term. On the other hand, when breathing techniques and AEs were combined only perceived stress improved. However, we did not identify any interaction in the intergroup effect. Moreover, significant differences were observed in the perception of change with treatment in favor of the FE group compared to the AE group. Quality of life reached the MCID for both groups.

Taking into account that fatigue is one of the most prevalent symptoms of long COVID-19,[47] our results are of great clinical relevance. Both groups, FE and AE, improved fatigue reaching the MCID after treatment but only the FE group showed statistical differences after the program. Although there have been significant efforts undertaken to explain the pathogenic mechanisms of fatigue in long COVID-19, the current knowledge is still scarce. It is probable that fatigue in long COVID-19 is due to a range of central, peripheral, and psychological factors .[48] Considering that

our FE program included strengthening exercises for the large muscle groups of both upper and lower limbs, it is probable that the involvement of these great muscle masses has increased the neuromuscular activity of the skeletal muscles.[49,50] This may have enhanced functional muscle strength[51] and explained the clinical and significant improvements observed in perceived fatigue. The AE group clinically improved in terms of fatigue, probably due to the incremental increase in aerobic capacity associated with walking endurance.[52]

Our results are in line with those of Ferraro et al,[53] who focused on patients who had COVID-19 and undertook a 6-week intervention that included strength exercises, breathing exercises, and training to walk progressive distances. This study observed there to be a decrease in fatigue and an improvement in exercise capacity.[53] Another study by Daynes et al[54] also found there to be improvements in exercise capacity and perceived fatigue after 6 weeks of strength exercises combined with AE and health education. However, these studies combined both strengthening and AEs, whereas our study has specifically focused on the effect of each treatment. Our intervention included breathing exercises that have previously shown to have benefits versus no rehabilitation in patients who overcame COVID-19,[55] and we combined them with either FE or AE in order to compare the effect of these 2 treatments. In addition, it must be considered that the measurement of fatigue has been generally poorly described.[56] However, we administered a validated multi-item fatigue questionnaire. Although some Fatigue Assessment Scale items assess physical fatigue and others mental fatigue, it is usually reported as a single domain. In fact, fatigue studies show that fatigue is one of the most prevalent symptoms in patients who have had COVID-19, and they have used the Fatigue Assessment Scale as a single domain.[57–59]

Regarding dyspnea in ADL, no significant or clinical changes were found. However, the scores at baseline were not considerably high and they were maintained after treatment in both groups. Other authors such as Li et al have reported an improvement in perceived dyspnea assessed using the modified Medical Research Council Scale. However, after discharge, patients who have had COVID-19 and moderate dyspnea were included, and the treatment combined breathing exercises, AE, and upper limb strength training; in addition, the sample size was larger.[9] In the same line, Nopp et al[60] also observed a decrease in dyspnea and an improvement of quality of life after a 6-week face-to-face intervention involving a combined treatment, specifically AE, strengthening, and respiratory muscle training. In addition, the participants in this study also received nutritional counselling and psychological support as part of their treatment. The National Institute for Health and Care Excellence recommendations suggest that dyspnea treatment and management should be multidisciplinary.[61] Future research on long COVID-19 should consider including the

collaboration of different health professionals (eg, a psychologist and/or psychiatrist) to enhance the benefits felt by the participants through a holistic approach.

It has been stated that after having COVID-19, up to one-third of people may have decreased functional capacity,[62] so it is an important variable to consider. In addition, our sample had a mean age of 42.4 years, which is an age of professional activity, meaning that a decrease in functional capacity could imply a high occupational impairment and a socioeconomic impact, although this was not registered. In a previous study with a smaller sample size,[6] functional performance was improved. However, unlike our study, aerobic and FEs were combined, so it was not elucidated which one had more of an effect on functional capacity. Our results showed that the FE group had a statistical improvement in the 30s-STS tests after treatment. This can be related to the strength gain previously stated, which not only influences fatigue and endurance but also functional performance.[63] Interestingly, both fatigue and functional performance significantly improved for the FE group. This is in line with the relationship that has been shown between these variables, thus muscular fatigue is associated with an impairment in motor performance both in relation to task difficulty and the ability to maintain force production.[64] Assessing both variables is important in the clinical context. In regard to perceived stress, both groups showed significant improvements between T1 and T2. COVID-19 is associated with chronic psychological stress, immune system dysregulation, and the stimulation of a hyperinflammatory state.[65] Cognitive behavioral therapy has shown to be effective in the treatment of stress, anxiety, and depression for this population.[66] This shows again the need for a global approach to patients with long COVID-19.

Our results have shown that exercise, both strengthening or aerobic, can improve stress, plus, the AE group improved clinically in terms of the depression variable. The explanation may be that exercise in general targets the neuropsychiatric and endocrine sequelae, modulating psychological stress. In fact, exercise training may lead to the adaptation of the responses to stressful stimuli.[65] Therefore, regular exercise in our population of patients with long COVID-19 has shown to play a key role in protecting against stress while also alleviating the symptoms of depression.[65] Moreover, both the FE and AE groups improved clinically in terms of their quality of life. Considering that it has been stated that patients with COVID-19 may have a poor health-related quality of life,[67] our results offer an affordable treatment to clinically improve it. In addition, fatigue has been associated with health-related quality of life in the medium term,[68] so again, clinicians should consider a holistic assessment and approach to the treatment of long COVID-19.

Another relevant finding of this study is that, regardless of the modality of work, rehabilitation using a mobile phone application has shown good levels of adherence to the treatment plan.

Regarding the instrument used, the patients rated the use of the Fisiotrack application with an excellent level of usability, regardless of the type of intervention assigned. On the other hand, it is important to mention that none of the treatment groups reported adverse events regarding the performance of the telerehabilitation exercise, suggesting that it is a safe tool if complemented with proper education by a trained health professional.

Limitations and Strengths

Among the main limitations of our study is the absence of a control group, which was not considered in this study since almost the entire target population had not had access to rehabilitation and had been waiting for months for an alternative treatment for the management of their symptoms. Additionally, only the short-term effects of the intervention were evaluated. Moreover, the use of self-reported assessments, such as the way adherence to treatment was recorded, could be a limitation. Despite these limitations, our results have shown that a physical therapist telerehabilitation program may be an effective nonpharmacological treatment option to improve the health of patients with long COVID-19, and depending on the main symptoms, functional or AE can be chosen. Future studies could consider the long-term effects of the treatment and the inclusion of other health professionals to extend these promising results.

Conclusions

Both telerehabilitation exercise modalities have excellent usability and are effective at improving stress symptoms and quality of life in patients with long COVID-19. However, for improving fatigue and functional performance, FE shows more promising results.

Authors' Contributions

Claudia Espinoza-Bravo (Data curation-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-Equal, Writing – original draft-Equal, Writing – review & editing-Equal), Anna Arnal-Gómez (Conceptualization-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-Equal, Writing – original draft-Equal, Writing – review & editing-Equal), Francisco Miguel Martínez-Arnau (Conceptualization-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-Equal, Writing – original draft-Equal, Writing – review & editing-Equal), Rodrigo Núñez-Cortés Data curation-Equal, Formal analysis-Equal, Investigation-Equal, Writing – original draft-Equal, Writing – review & editing-Equal David Hernández-Guillén (Investigation-Equal, Methodology-Equal, Writing – original draft-Equal, Writing – review & editing-Equal), Cristina

Flor-Rufino (Investigation-Equal, Methodology-Equal, Writing – original draft-Equal, Writing – review & editing-Equal), Sara Cortés-Amador (Conceptualization-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-Equal, Project administration-Equal, Supervision-Equal, Writing – original draft-Equal, Writing – review & editing-Equal)

Acknowledgments

The authors << Q9 - Query: Per style, please provide authors' contributions section, if any. Ans: **anna.arnal@uv.es:** After "Conclusions" and before "Acknowledgments" there is already and "Authors Contributions section". >>gratefully acknowledge the use of the Fisiotrack mobile phone application. The authors especially thank all the participants for taking part in the study.

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest, financial or otherwise.

Conflict of Interest: the authors report no conflict of interest.

Data availability: data are available under reasonable request.

FUNDING: There are no funders to report for this study.

Clinical Trial Registration

The study protocol was registered prospectively on ClinicalTrials.gov (NCT04996212).

Supplementary Data

Supplementary data for this article are available at *PHYSTH* online.<< Q10 - Query: Please provide a Funding statement, detailing any funding received. Remember that any funding used while completing this work should be highlighted in a separate Funding section. Please ensure that you use the full official name of the funding body, and if your paper has received funding from any institution, such as NIH, please inform us of the grant number to go into the funding section. We use the institution names to tag NIHfunded articles so they are deposited at PMC. Ans: **anna.arnal@uv.es:** Thank you, we have provided it. >>

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Queries

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Q1	Please check the spelling and accuracy of all author names and affiliations, particularly for any of your coauthors. Please also check that author surnames are correctly identified with a pink background. This is to ensure that forenames and surnames are tagged correctly for online indexing. {\bfseries Incorrect names and affiliations may lead to an author not being credited for their work by funders, institutions, or other third parties.}	Author	anna.arnal@uv.es	Author	We have checked, names and affiliations are correct.
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Q3	Please check that funding is recorded in a separate funding section if applicable. Use the full official names of any funding bodies, and include any grant numbers.	Author	anna.arnal@uv.es	Author	There was no funding for this study, so it is not applicable. However, we have stated this in a section at the end of the manuscript.

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Q4	You may need to include a “conflict of interest” section. This would cover any situations that might raise any questions of bias in your work and in your article’s conclusions, implications, or opinions. Please see here https://academic.oup.com/journals/pages/authors/authors_faqs/conflicts_of_interest.	Author	anna.arnal@uv.es	Author	Thank you, we have included at the end of the manuscript a Conflict of Interest Section.
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Q6	Author names are mismatch between Swift xml and MSP. I have followed MSP. Please check and confirm.	Author	anna.arnal@uv.es	Author	Authors are correct as shown in the Proof and how we send it to the journal which was as follow: Claudia Espinoza-Bravo, PT, MSc, Anna Arnal-Gómez*, PT, PhD, Francisco Miguel Martínez-Arnau, PT, PhD, Rodrigo Núñez-Cortés PT, MSc, David Hernández-Guillén,PT, PhD, Cristina Flor-Rufino, PT, PhD, Sara Cortés-Amador, PT, PhD.

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Q7	Please provide the department name in affiliation 1.	Author	anna.arnal@uv.es	Author	The department for Affiliation 1 is as follows: Home Hospitalisation Unit.
Q8	Please provide the state and postal code details in all the affiliations.	Author	anna.arnal@uv.es	Author	We provide this information here: - Day Hospital Unit, Home Hospitalisation Unit, Hospital Clínico la Florida, 8240000 Santiago, Chile. - Department of Physiotherapy, Faculty of Physiotherapy, University of Valencia, 46010, Valencia, Spain. - Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), Department of Physiotherapy, Faculty of Physiotherapy, University of Valencia, 46010, Valencia, Spain. - Department of Physical Therapy, Faculty of Medicine, University of Chile, 8240000, Santiago, Chile. - Group of Physiotherapy in the Aging Process: Social and Health Care Strategies (PT_AGE), Department of Physiotherapy, Faculty of Physiotherapy, 46010, Valencia, Spain.
Q9	Per style, please provide authors' contributions section, if any.	Author	anna.arnal@uv.es	Author	After "Conclusions" and before "Acknowledgments" there is already and "Authors Contributions section".
Q10	Please provide a Funding statement, detailing any funding received. Remember that any funding	Author	anna.arnal@uv.es	Author	Thank you, we have provided it.

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	used while completing this work should be highlighted in a separate Funding section. Please ensure that you use the full official name of the funding body, and if your paper has received funding from any institution, such as NIH, please inform us of the grant number to go into the funding section. We use the institution names to tag NIHfunded articles so they are deposited at PMC.				
Q11	Please provide the author(s) name(s), publisher name , publisher location and accessed date for reference 1.	Author	anna.arnal@uv.es	Author	Thank you, we have added information for this reference: World Health Organization. WHO Coronavirus (COVID-19) Dashboard. [cited 2022 Dec 3]; https://covid19.who.int/.[Accessed 2022 Nov 6]
Q12	References [1–21, 23–52, 54–68] were provided in the reference list; however, this was not mentioned or cited in the manuscript. As a rule, all references given in the list of references should be cited in the main body. Please provide its citation in the body text.	Author	anna.arnal@uv.es	Author	We have reviewed the mentioned references, we do see them cited in the manuscript. As examples, Reference 1 is in the first paragraph of introduction, reference 21 in the second paragraph of methods, reference 52 is correctly in the second paragraph of the discussion. We can see in the Proof all the references cited in the main body text. However, we have noticed reference 8 and 10 (at the end of the first

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					paragraph of introduction) are not correctly linked, they should be cited at the end of first paragraph, in the superscript were it says "7-10", we have added the link to reference 8 but we can not add the one of reference 10: 8. do Amaral VT, do Amaral VT, Viana AA, et al. Cardiovascular, Respiratory, and Functional Effects of Home-Based Exercise Training after COVID-19 Hospitalization. Medicine & Science in Sports & Exercise 54(11):p 1795-1803, November 2022. | DOI: 10.1249/MSS.0000000000002977. 10. Udina C, Ars J, Morandi A, Vilaró J, Cáceres C, Inzitari M. Rehabilitation in adult post-COVID-19 patients in post-acute care with therapeutic exercise. J Frailty Aging. 2021;10:297–300. https://doi.org/10.14283/jfa.2021.1.
Q13	Please provide the page range for references 6, 23.	Author	anna.arnal@uv.es	Author	We have provided page range for reference 6, which now reads: - Estebanez-Pérez M-J, Pastora-Bernal J-M, Martín-Valero R. The effectiveness of a four-week digital physiotherapy intervention to improve functional capacity and adherence to intervention in patients with long COVID-19. Int J Environ Res Public Health [Internet]. 2022;19: 9566. https://doi.org/10.3390/ijerph19159566.

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					However, for reference 23 the page range is what it shows already: g1687, we could not find further information.
Q14	Please provide the volume, page range, journal title for references 8, 45, 47.	Author	anna.arnal@uv.es	Author	For reference 8 the information is as follows: 8. TEIXEIRA DO AMARAL, VANESSA; VIANA, ARIANE APARECIDA; HEUBEL, ALESSANDRO DOMINGUES; LINARES, STEPHANIE NOGUEIRA; MARTINELLI, BRUNO; WITZLER, PEDRO HENRIQUE CAMPRIGHER; ORIKASSA DE OLIVEIRA, GUSTAVO YUDI; ZANINI, GABRIEL DE SOUZA; BORGHI SILVA, AUDREY; MENDES, RENATA GONÇALVES; CIOLAC, EMMANUEL GOMES. Cardiovascular, Respiratory, and Functional Effects of Home-Based Exercise Training after COVID-19 Hospitalization. Medicine & Science in Sports & Exercise 54(11):p 1795-1803, November 2022. | DOI: 10.1249/MSS.0000000000002977 For reference 45 it is as follows: 45. Sevilla-Gonzalez, M. D. R., Moreno Loaeza, L., Lazaro-Carrera, L. S., Bourguet Ramirez, B., Vázquez Rodríguez, A., Peralta-Pedrero, M. L., & Almeda-Valdes, P. (2020). Spanish Version of the System Usability Scale for the Assessment of Electronic Tools: Development and Validation. JMIR human factors, 7(4), e21161. https://doi.org/

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					10.2196/21161 For reference 47 the information is as follows: 47. Davis, H. E., Assaf, G. S., McCorkell, L., Wei, H., Low, R. J., Re'em, Y., Redfield, S., Austin, J. P., & Akrami, A. (2021). Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine, 38, 101019. https://doi.org/10.1016/j.eclinm.2021.101019
Q15	Please provide the author(s) name(s) and year for reference 61.	Author	anna.arnal@uv.es	Author	Thank you, we have provided the authors name: National Institute for Health and Care Excellence. COVID-19 Rapid Guideline: Managing the Long-Term Effects of COVID-19. London: National Institute for Health and Care Excellence (NICE). Available from: nice.org.uk/ng188. Accessed: 2022 Nov 20.
Q16	Please provide the volume number for reference 66.	Author	anna.arnal@uv.es	Author	When the volume number is added the reference is as follows: Li, J., Li, X., Jiang, J., Xu, X., Wu, J., Xu, Y., Lin, X., Hall, J., Xu, H., Xu, J., & Xu, X. (2020). The Effect of Cognitive Behavioral Therapy on Depression, Anxiety, and Stress in Patients With COVID-19: A Randomized Controlled Trial. Frontiers in psychiatry, 11, 580827. https://doi.org/10.3389/fpsyt.2020.580827
Q17	Please provide the volume number, page range	Author	anna.arnal@uv.es	Author	The reference 68 does not have yet a number or page range because up

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