Effects and feasibility of a supervised exercise program plus multimodal home-based exercises post-hospitalized COVID-19 individuals.

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ABSTRACT
introduction: Exercise programs have been recommended to individuals with persistent symptoms after COVID-19 hospital discharge. Aim: The objective of this research was to analyze the effects and feasibility of an 8-week supervised high intensity endurance and strength training plus multimodal home-based exercise program on physical, functional outcomes, levels of anxiety and in individuals with persistent symptoms after COVID-19 hospital discharge. Methods: This non-randomized study with convenience sampling, included adults reporting muscle weakness, dyspnea, and/or fatigue after COVID-19 hospitalization, with significant limitations. Exercise program included supervised high-intensity resistance and strength training sessions, as well as multimodal home exercises. The assessed outcomes included pulmonary function (spirometry), exercise capacity (6MWT); functionality capacity (STS-1min) and Post-COVID Functional Scale (PCFS), handgrip strength (HGS) and one-repetition maximum (1RM), quality of life (SF-36); and levels of anxiety and depression (total HADS). Feasibility was achieved if 50% of the sample completed 90% of the sessions of the program. Results: After intervention, individuals improved FVC, FEV1, 6MWT, STS-1mim, HGS; 1RM, SF-36 and total HADS (P< 0.005 for all results). In addition, in PCFS, 100% of the individuals showed significant improvement after intervention compared with previous functional status p<0.0001. Study retention was 66% (22 of the 33 participants), mean adherence over the 8 weeks was 90%. No adverse events were reported. Conclusion: Supervised high intensity endurance and strength training plus multimodal home-based exercise improved the functional capacity, muscle strength, symptoms of anxiety, and functional status in post-hospitalized COVID-19 patients, demonstrated its application to be feasible and safe
.Key words: Post Covid-19; Multimodal exercise program; Rehabilitation.

Introduction

The COVID-19 pandemic caused by the SARS-CoV-2 virus (Severe Acute Respiratory Syndrome-related Coronavirus-2) produced negative consequences for public health worldwide. Individuals infected by SARS-CoV-2 virus presented symptomatic manifestations such as fever, cough, headache, sore throat, dyspnea, diarrhea, myalgia, and vomiting (1). Depending on the severity of the case, patients experienced respiratory difficulty, hypoxia, respiratory failure and consequently the need for mechanical ventilation and hospitalization in the critical care unit. For this reason, the majority of individuals who survived the hospitalization period after COVID-19 presented different physical and functional sequelae and from 27% to 79% of the individuals required physical rehabilitation (2).
The length of hospitalization for SARS-CoV-2 virus was associated to serious systemic impairments. Critically ill patients often experience persistent symptoms for days or even months after hospital discharge, involving physical and psychological sequelae, affecting their quality of life. The presence of theses persistent symptoms is called post covid syndrome (3). For those individuals who still had symptoms after the hospital phase, it was observed the need for intervention to reinsert them to their basic activities of daily living, work activities and management of symptom control on health-related quality of life, which was directly impacted by the functional clinical picture (2). To improve this functional impact, rehabilitation during hospitalization and after discharge is highly recommended in individuals

with COVID-19. Targeted rehabilitation in post-COVID-19 patients is important due to the pulmonary and extrapulmonary deleterious effects that may persist after the infection in most of the individuals withCOVID-19(4)

The rehabilitation programs designed to individuals with COVID-19 have been based on previous guidelines for other chronic respiratory diseases, including passive and active-assisted exercises, secretions removal techniques and respiratory exercises. However, since the sequelae of COVID-19 are not only related to lung function, multimodal exercises that include aerobic, strength, flexibility and balance exercises would be more recommendable. Rehabilitation programs including multimodal exercise training in this field are scarce and their functional effects on individuals affected by this disease are not yet fully understood. Most of the modality programs reported in the literature include supervised exercise programs with strength, aerobicor balance training, however theses intervention programs are generally not combined with home-based exercise programs (2). Home-based exercise appears affective to improve functional and health outcomes in individuals with COVID-19(5), also being observed exercises in the form of telerehabilitation (6). For this reason, the aim of this study was to compare the effects and feasibility of a supervised high intensity endurance and strength training plus multimodal home-based exercise program on physical and functional outcomes in individuals' post-hospitalization due to COVID-19.

Material And Methods

Study Design And Participants

This is a non-randomized study with a convenience sampling. The individuals included in the study were recruited through social media, radio, and television in the city of Londrina, Brazil. The announcement invited individuals of both genders, over 18 years old, with complaints of muscle weakness, dyspnea, and/or fatigue following hospitalization due to COVID-19, to participate in a physical and functional assessment at the Physiotherapy Outpatient Clinic of the University Hospital of the State University of Londrina, Brazil. After the tests, those who presented significant limitations, based on the reference values of the tests in question, could be included in the exercise program at the same outpatient clinic. Individuals with decompensated underlying diseases, severe exacerbations that prevented treatment continuity, or participants who wished to discontinue the study were excluded.

A total of 101 individuals were recruited for the study. Among them, 46 individuals started the assessment tests and 33 completed it and started the proposed training program, and 22 successfully completed it. The study flowchart can be found in Figure 1. All individuals included in the study signed the Informed Consent Form. The study was approved by the Institutional Research Ethics Committee (Approval number 4,327,528).

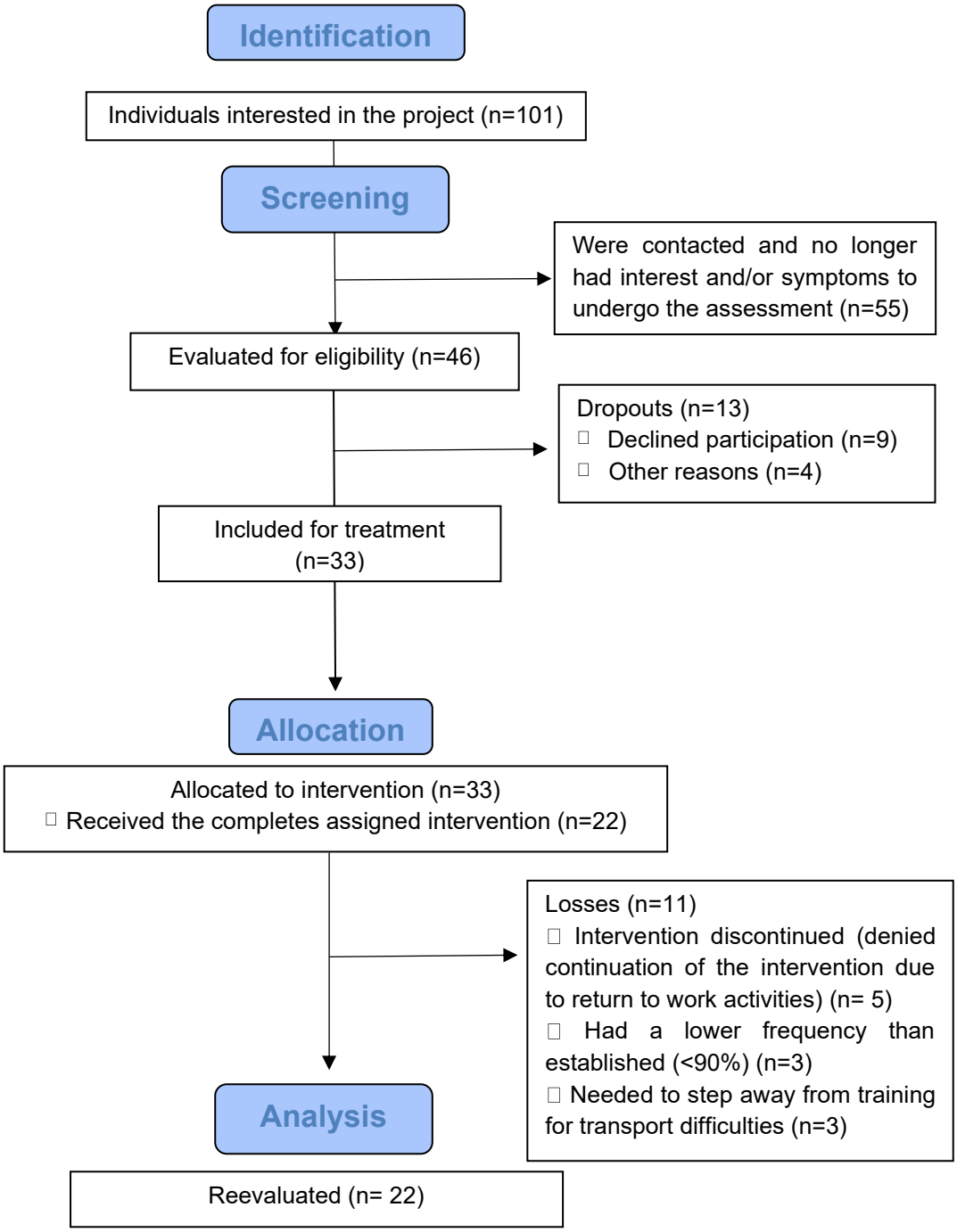

Figure 1. Study patient inclusion flowchart

Procedures

A full physical and functional assessment was conducted over three days at the outpatient clinic. On the first day of assessment, individuals completed a questionnaire that included personal information, anthropometric data, past and current health history and medication use. In addition, lung function and muscle strength were also measured. Exercise capacity, functionality, quality of life and symptoms of anxiety and depression were evaluated on a second visit. Finally, the last day of evaluation included other muscle strength measurements. Detailed information and the instruments used in the assessed outcomes are provided below.

Pulmonary Function

Evaluated through Spirometry test using a portable digital spirometer model Spirobank II (ADVANCED® - MIR, Italy), both pre- and post-bronchodilator, following the international criteria of the American Thoracic Society (ATS) and the European Respiratory Society. The reference values used were specific to the Brazilian population (7).

Exercise Capacity

The 6-minute walk test (6MWT) was used. The test was conducted according to international guidelines in a 30-meter corridor. Two tests were performed with a minimum interval of 30 minutes between them, and the best value was used for analysis. The reference values used were those established by Britto et al.(8).

Functionality

Functionality was assessed objectively using the 1-minute sit-to-stand test (STS-1min) and subjectively using the Post-COVID-19 Functional Status Scale (PCFS). The STS-1min test focuses on a common daily movement, which is sitting and standing up. The protocol used was based on Strassmann et al. (9), in which the individual being evaluated needs to sit and stand up from a chair without any support as many times as possible within one minute. The number of repetitions achieved is the outcome measured, following the protocol and its reference values for each age group and gender. To assess the impact of COVID-19 on functional status, the PCFS was utilized. It is an ordinal scale created to evaluate the course of symptoms in functional outcomes, focusing on limitations in daily tasks, sports activities, and social activities. The scale is composed of two parts, with limitation scores ranging from 0 to 4, and is expressed in the form of a patient questionnaire and a flowchart, where both were applied and their values were considered, with the highest degree of the score being used, considering the greatest limitations. A score of 0 represents no functional limitations, while a score of 4 indicates severe functional limitations, and a score of 5 indicates a risk of death (10). The PCFS is recommended for application at the time of hospital discharge up to four to eight weeks post-discharge to monitor direct recovery. It is also recommended to assess functional sequelae at six months after the discharge. This allows for the monitoring of functional status over time and the evaluation of the long-term impact of COVID-19 on an individual's functional abilities. For its application, under supervision and guidance, the patient was instructed to select the appropriate level on the PCFS based on their current condition at the time of assessment. They would follow the levels of impairment outlined in the scale's flowchart. In cases where two gradations appeared to be appropriate, the patient would mark the one indicating greater limitation. This process ensured that the patient's functional status was accurately reflected in their assessment on the PCFS.

Muscle Strength

Muscle strength was evaluated through handgrip strength (HGS) and one-repetition maximum (1RM) testing. Handgrip strength was assessed by measuring isometric contraction in both hands using a portable digital dynamometer, specifically the Jamar Plus+ model (Jamar® 12-0604 Digital Dynamometer, Petterson Medical, USA). The one-repetition maximum (1RM) test was used to assess isotonic concentric muscle strength. This test measures the individual's ability to lift the heaviest weight through the full range of motion without any postural compensation.

The test was used to determine the load to be used in strength training and to assess muscle strength before and after treatment. On the final day of assessment for determining the 1RM, the patient underwent an equipment adaptation phase, which consisted of performing one repetition without any load, followed by a progressive protocol until the maximum load was lifted through the full range of motion for each muscle group assessed on the multi-station strength training equipment (CRW 1000; Embreex, Brusque, Brazil). The following muscle groups were evaluated: latissimus dorsi, pectoralis, biceps, triceps, and quadriceps (LD, PT, BC, TC, QD, respectively) (11).

Quality of Life

Health-related quality of life was measured using the Brazilian version of the Short Form Health Survey (SF-36) questionnaire, being a multidimensional instrument, the SF-36 questionnaire is short, easy to administer, and understand. The abbreviated questionnaire consists of 36 questions, divided into eight domains that cover functional capacity (10 items), physical aspects (4 items), pain (2 items), general health (5 items), vitality (4 items), social aspects (2 items), emotional aspects (3 items), and mental health (5 items). Additionally, two summary measures, the Physical Component Summary (PCS) and Mental Component Summary (MCS), are derived from the questionnaire. The calculation of domain scores in accordance with the recommendations of the SF-36 developers. The final score for each domain can range from 0 to 100, where 0 represents the poorest overall health status and 100 represents the best health status (12).

Anxiety and Depression

The presence of symptoms of anxiety and depression was assessed using the Hospital Anxiety and Depression Scale (HADS). The instrument consists of 14 questions, divided equally into 2 domains: HADS-Anxiety (HADS-A) (odd-numbered items) and HADS-Depression (HADS-D). Each question is scored from 0 to 3 (from absent to very frequent), and the total score for each subscale ranges from 0 to 21. A score below 7 indicates a mild presence of depressive or anxious symptoms, a score between 8 and 10 indicates a possible case of depression or anxiety, and a score between 11 and 21 indicates a probable case (13).

Supervised exercise program

After comprehensive evaluation, the supervised rehabilitation program and a structured exercise regimen for home-based training was initiated, which lasted for a period of eight weeks. The training sessions took place three times a week, with two days of supervised training at the outpatient clinic and one day of home-based training with guidance, totaling 24 sessions.

The supervised sessions included high intensity endurance and strength training, protocol followed by international guidelines and recommendations for established pulmonary diseases as pre-established in the literature (14). Each session lasted 50 minutes. The progression of the exercise's intensity was based on the performance of the initial assessments, specifically the 6MWT and the 1RM. Walking exercise was performed at an intensity of 75% of the initial 6MWT gait speed during 10 minutes, aiming to reach 95% of the speed by the 8th week of training during 16 minutes. As a complement to aerobic training, an ergometric bicycle was used estimating the maximum working watts from the measurement of 6-minute walk distance based on the formula of Hill K et al. (15), which is a basis for the workloads, in accordance with the current guidelines for pulmonary rehabilitation, and its progression weekly with an initial intensity of 60% of the maximum workload based on the distance on 6MWT during 10 minutes, with the goal of reaching 80% of the maximum load in the same training period during 16 minutes. Vital signs, including blood pressure, heart rate, and peripheral oxygen saturation, were monitored at the beginning, during and at the end of each supervised outpatient session to ensure safety and well-being of the participants.

The progression of exercises was also based on the symptoms of dyspnea and muscle fatigue,

assessed using the Borg Rating of Perceived Exertion Scale. Adjustments were made according to the subjects' perception of dyspnea and fatigue using the modified Borg Scale (0-10), with the target training range between 4 and 6 (16). For strength training exercises, individuals performed 3 sets of 8 to 12 repetitions with an initial load of 70% of the 1RM test for the assessed muscles. The goal was to increase the load by 6% per week, aiming to reach 106% of the 1RM test at the end of the 8-week program. Each exercise was performed according to the endurance capacity of each patient, allowing for rest intervals during a set if necessary to complete it. For individuals who presented saturation levels below 88% during the sessions, supplemental oxygen was provided via nasal cannula. The progression of the proposed protocol is described in Figure 2.

Multimodal home-based training

For the multimodal complementary home training, an informative and descriptive booklet on home exercises was provided to each patient. Maximum repetition tests for each exercise were performed at the time of delivery, and the highest number of repetitions was performed in each exercise that required repetitions (exercise 3 and 4). The number of repetitions for this exercise varied according to the week of training, starting at 75% of the initial test in the first and second weeks, 85% in the third and fourth weeks, 95% in the fifth and sixth weeks, and 105% in the seventh and eighth weeks of training. The booklet contained instructions on how to do it, with safety instructions and exercise modifications (Figure 3), and a specific day was agreed upon for each patient to undergo home training, with a day of rest after the outpatient session. The booklet contained four functional exercises with images and instructions on how to perform them, including 1) one-legged balance exercises, 2) general stretching, 3) stationary gait, and 4) sit-and-stand exercise, with their individualized progression based on each patient's initial test (Figure 2). During the home training session, each patient was instructed to follow the order of exercises, and each exercise was performed in 3 sets, with a one-minute rest between each set. To monitor the execution of home exercises, the Borg Scale for Fatigue and Dyspnea was filled out after performing the exercises in the home booklet, and it was checked weekly by the clinic's physiotherapists. In addition, a physiotherapist was tasked with contacting the patient on the agreed-upon day for exercise execution to remind them of their activities. Each session lasted 35 to 40 minutes.

After the entire training period, each participant who completed the proposed Physical and Functional Training Program underwent a reassessment using the same tests as in the initial evaluation to compare their results. They received comparative feedback on some of the tests before and after the 8-week intervention. The primary outcome of the study was the changes in the tests before and after the intervention.

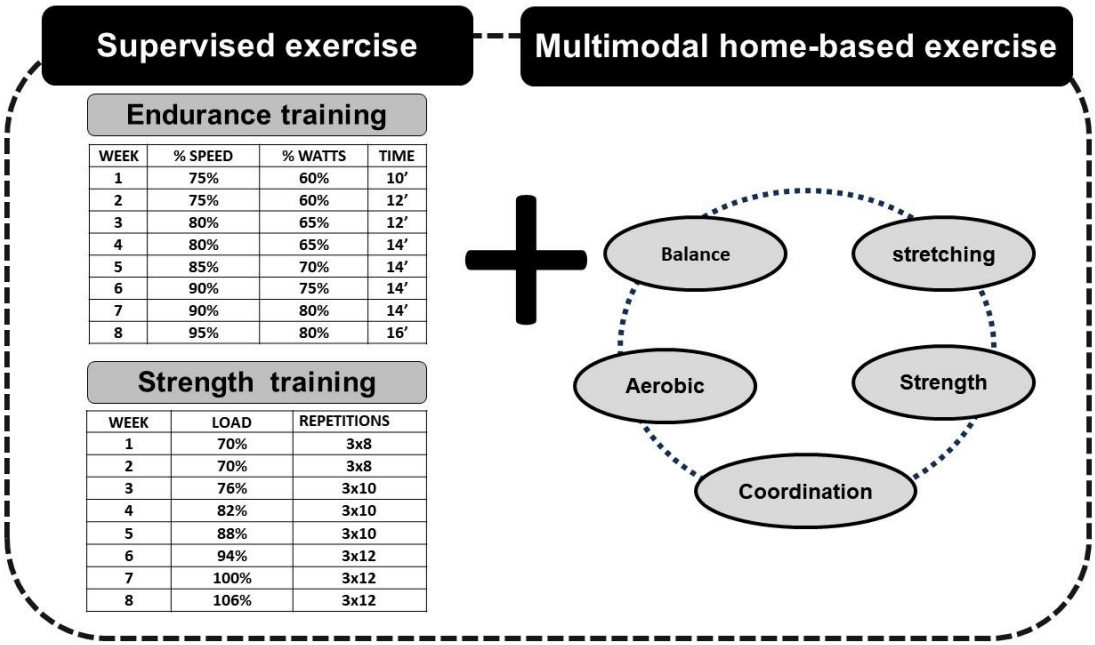

Figure 2. Exercise program.

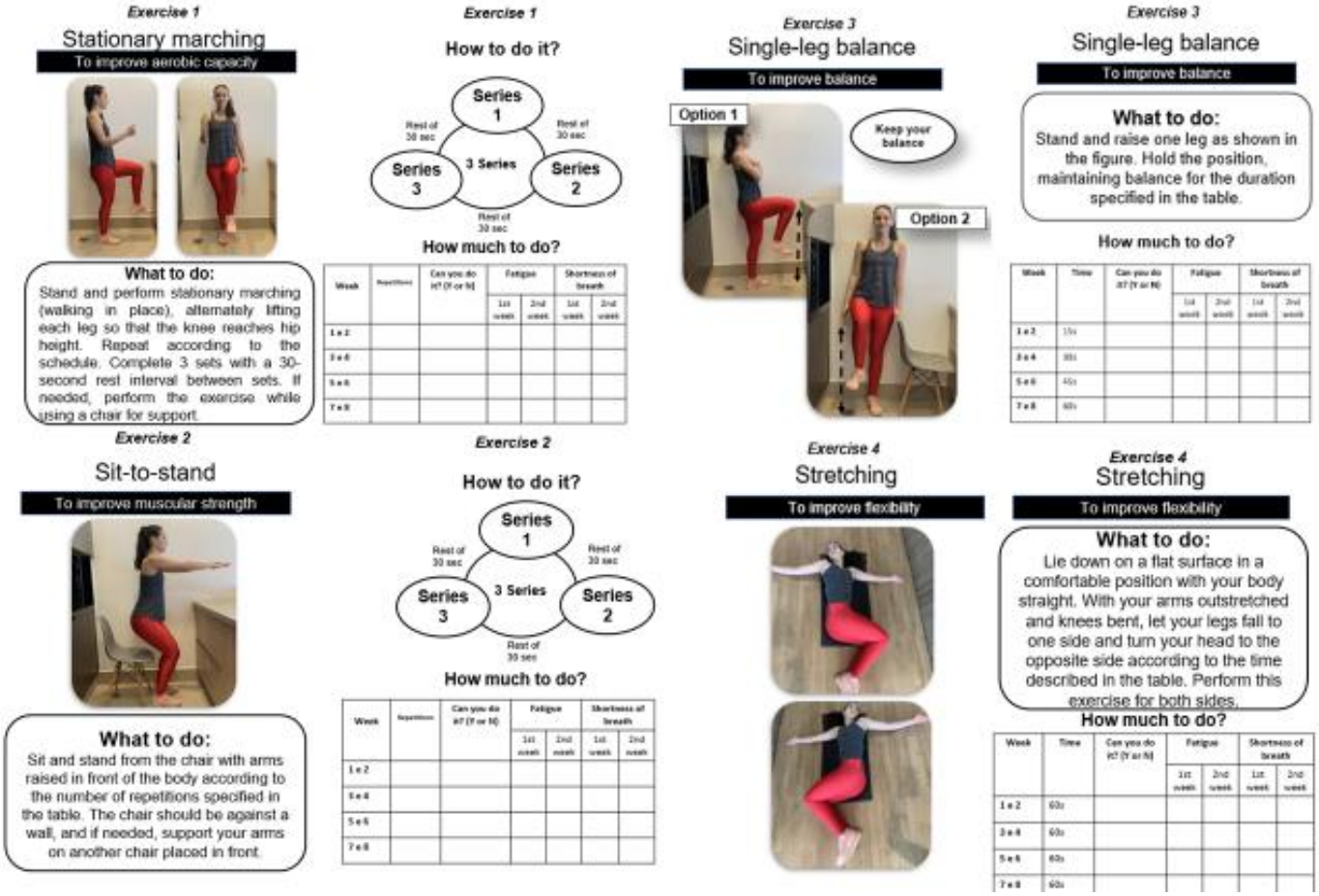

Figure 3. Booklet on home exercises.

Feasibility outcomes

Retention was recorded as the number (proportion) of participants who completed the 8-week program. Adherence to the exercise program, including the number of sessions completed, number of exercises, and sets and repetitions completed (all expressed as a percentage) within each session were recorded within the internal evolution health system. Total adherence (100%) was defined as the participant who performed the exercises three days a week (collecting the information derived from the weekly record booklet of the home exercises). We considered the program to be feasible if at least 50% of the participants completed 90% of the sessions of the program (17). Participants were weekly asked about any adverse events (including falls) by the research staff. An adverse event was defined as an intervention-related event resulting in absence from or modification to the exercise intervention, vital signs data (systemic blood pressure, peripheral oxygen saturation, heart rate, modified Borg dyspnea scale, and fatigue) were assessed during outpatient training sessions, following a patient safety protocol.

Statistical analysis

Statistical analysis was conducted to evaluate significant differences in outcomes between before and after the effects of the intervention group. The analysis was performed using SPSS 25.0.0 for Windows (IBM® SPSS® Statistics, Armonk, NY: IBM Corp., 2007). The comparison of outcomes before and after the ambulatory training program was conducted using paired Student's t-test (parametric data) and Wilcoxon test (non-parametric data) analyzed according to data normality. Statistical significance was considered at $p < 0.05$. Finally, we calculated Cohen's effect size (ES) for the effect of intervention, considering the effect to be trivial (<0.2), small (0.2–0.5), medium (0.5–0.8) or large (>0.8) (18).

RESULTS

In total, out of the 46 patients who started the evaluation, 45 completed it in its entirety. Among them, 9 individuals were not interested in starting the treatment, and 4 individuals did not show a significant decline in functional tests that warranted intervention. As a result, according to the feasibility, 33 individuals began the training program, and among them, 11 (33%) did not complete at least 90% of the training sessions (Figure 1). Study retention was 66% (22 of the 33 participants) completed the study, mean adherence over the 8 weeks was higher than 90% (Table 1).

Exercise adherence during the 2 weeks was 100%, consecutively having three dropouts in the 3rd week, two in the 4th week, one in the 5th, two in the 6th, and one in the 7th week of intervention, and two dropouts after the 7th week. Among those subjects who dropped out during the program, the primary reason was a sense of recovery, coupled with the need to return to work and also difficulties related to transport to the training facility. No adverse events were reported by subjects during the exercise programs, demonstrating its safety.

Regarding the sample characteristics (Table 1), the majority were men (68%), with a mean age of young adults at 45 years old, and a mean BMI classification of obese at 29kg/m². Evaluating educational level, most individuals had completed higher education (50%) and were in active work phase (77%). In terms of hospitalization data, the median length of hospital stay was 13 days, where the majority of individuals (64%) required intensive care in the ICU, with the same rate found among those who required prone positioning (64%). Additionally, 45% of the sample was intubated and benefited from invasive mechanical ventilation. Compared to hospital discharge at the start of the evaluation, the median number of days was 27, ranging from 12 to 64 days.

Table 1. General characteristics and historical characteristics of hospitalization of patients included in the study (n=22)

Variables	Results
Gender, M/F (n [%])	15/7 [68/32]
Age (years)	45±15
Height (m)	1,70±0,09
Body Mass (Kg)	86±18
BMI (kg/m^2)	29±4
Education level (n [%])	
Elementary Education Incomplete/Complete	1/1 [4,5/4,5]
High School Education Incomplete	7 [32]
Higher Education Incomplete/Complete	2/11 [9/50]
Works/Retired/Student (n [%])	16/4/2 [77/18/5]
Length of hospital stay (days)	13 [8-39]
Need for ICU (yes/no)	14/8
Pronation position (yes/no)	14/8
Mechanical ventilation (yes/no)	10/12
Tracheostomy (yes/no)	6/16
Time between discharge and evaluation (days)	27 [12-64]

M: male; F: female; m: meters; kg: kilograms; BMI: body mass index. The values of the categorical variable were described in frequency (percentage) and numerical variables in mean and standard deviation, according to the normality of data distribution.

The results of the study showed significant improvements in various outcomes following the outpatient training program. There was a significant increase in 6MWT (ES: 1.55; CI 95%: 0.92-2.17; <0.0001), STS1min (ES: 1.06; CI 95%: 0.52-1.57; <0.0001), HGF (ES: 1.14; CI 95%: 0.59-1.67; <0.0001) and 1RM PT (ES: 1.87; CI 95%: 1.16-2.57; <0.0001), LD (ES: 1.36; CI 95%: 0.77-1.94; <0.0001), TC (ES: 1.30; CI 95%: 0.72-1.86; <0.0001), BC (ES: 1.70; CI 95%: 1.03-2.34; <0.0001), and QD (ES: 1.40; CI 95%: 0.80-1.98; <0.0001). Furthermore, there was a significant improvement in health-related quality of life, as assessed by the SF-36 questionnaire in the subtopics Functional Capacity (ES: 1.32; CI 95%: 0.74-1.89; <0.0001), Limitations due to physical aspects (ES: 1.60; CI 95%: 0.95-2.22; <0.0001), Vitality (ES: 0.80; CI 95%: 0.31-1.27; <0.001), Social Aspects (ES: 0.73; CI 95%: 0.25-1.19; <0.005R), and Mental Health (ES: 0,50; CI 95%: 0,05- 0,94; <0,05). Regarding symptoms of anxiety and depression, there was a significant reduction in score on anxiety HADS, indicating a decrease in symptoms throughout the training program (Table 2). Finally, 100% of the individuals showed significant improvement in PCFS (p<0.0001), after the exercise program, most individuals presented slight, negligible, or not limitations (Figure 3).

Regarding the effect size of the intervention, most findings focused on large variations where we had findings with effect sizes >0.8: STS 1 min ES 1.06; 6MWT (m) and 6MWT (% pred) ES 1.55; HGS (Kg) ES 1.14; 1RM PT ES 1.87; 1RM LD ES 1.36, 1RM TC ES 1.30, 1RM BC ES 1.70, 1RM QD ES 1.40; FVC (% pred) ES 1.04; FEV1 (L) ES 1.01, FEV1 (% pred) ES 1.08; SF-36 Functional capacity ES 1.32, Limitation due to physical aspects ES 1.60; PCFS ES 1.51. This is followed by small effect size (0.2–0.5) (with 6 variables): FEV1/CVF (%) ES 0.28; SF-36 Pain ES 0.42, General health status ES 0.31, Mental health ES 0.05; HADS Depression ES 0.27; HADS ES 0.44. With moderate effect (3 variables): SF-36 Vitality ES 0.80, Social aspects ES 0.73; HADS Anxiety ES 0.55. And trivial effect size (2 variables): FVC (L) ES 0.10; and SF-36 Limitation due to emotional aspects ES 0.08; demonstrated strong improvements regarding the intervention.

The magnitude of the difference pre and post-intervention, among the variables evaluated, ranged from 16 to 72% in those that were considered statistically significant.

Table 2. Results of exercise capacity, functionality, muscle strength, pulmonary function and quality of life related to health and symptoms of anxiety and depression, before and after intervention (n=22)

VARIABLES	Pre	Post	*P*	*Effect Size*	*IC 95%*	
STS 1 min (rep)	19[14-23]	26[23-30]	<0,0001	1,06	0,52	1,57
6MWT (m)	490±122	582±95	<0,0001	1,55	0,91	2,16
6MWT (% pred)	85±21	99±17	<0,0001	1,55	0,92	2,17
HGS (Kg)	34±15	41±13	<0,0001	1,14	0,59	1,67
1RM PT	18±10	31±15	<0,0001	1,87	1,16	2,57
1RM LD	26[19-33]	36[23-45]	<0,0001	1,36	0,77	1,94
1RM TC	17±6	26±11	<0,0001	1,30	0,72	1,86
1RM BC	15±7	22±8	<0,0001	1,70	1,03	2,34
1RM QD	24±12	36±13	<0,0001	1,40	0,80	1,98
FEV_1/CVF(%)	86,11±5,01	84,50±6,38	0,098	0,28	0,15	0,71
FVC (L)	3,16[2,51-3,42]	3,43[2,39-3,65]	0,705	0,10	0,32	0,52
FVC (% pred)	74,5[61-79]	84,5[75-102]	<0,001	1,04	0,51	1,55
FEV_1 (L)	2,59[2,22- 3,08]	3,44[2,39-3,7]	<0,001	1,01	0,49	1,52
FEV_1 (% pred)	77,77±15,34	92,27±16,17	<0,001	1,08	0,54	1,60
SF-36						
Functional capacity	48[30-61]	80[71-90]	<0,0001	1,32	0,74	1,89
Limitation due to physical aspects	0[0-0]	88[44-100]	<0,0001	1,60	0,95	2,22
Pain	53±29	64±23	0,07	0,42	0,85	0,02
General health status	70[56-87]	82[56-92]	0,13	0,31	-0,73	0,12
Vitality	53[44-60]	63[50-76]	0,0016	0,80	0,31	1,27
Social aspects	57[25-78]	82[63-100]	0,0059	0,73	0,25	1,19
Limitation due to emotional aspects	33[0-100]	33[0-100]	0,690	0,08	-0,34	0,50
Mental health	57±21	66±21	0,035	0,50	0,05	0,94
HADS						

Anxiety	6[4-10]	4[2-9]	0,02	0,55	0,10	0,10
Depression	5[2-9]	4[2-6]	0,11	0,27	-0,16	0,69
Total	13±8	10±7	0,27	0,44	-0,05	0,88
PCFS	3[2-3]	1[0-2]	<0,0001	1,51	0,89	2,12

Data is presented as mean and standard deviation (SD) and median and interquartile range (IQR; 25%-75%) according to data normality distribution. STS 1 min: Sit to Stand one minute; rep: number of repetitions; % pred: percentage of predicted value; 6MWT: Six minute walk test; m: meters; HGS: handgrip strength; Kg: kilograms; 1RM: one-repetition maximum test; PT: pectoralis; LD: latissimus dorsi; TC: triceps, BC: biceps, QD: quadriceps; FEV1: Forced expiratory volume in the first second, FVC: Forced vital capacity; L: liters; pred: predicted. SF-36: Short Form Health Survey (SF-36); HADS: Hospital Anxiety and Depression Scale (HADS); PCFS: Post COVID Functional Scale.

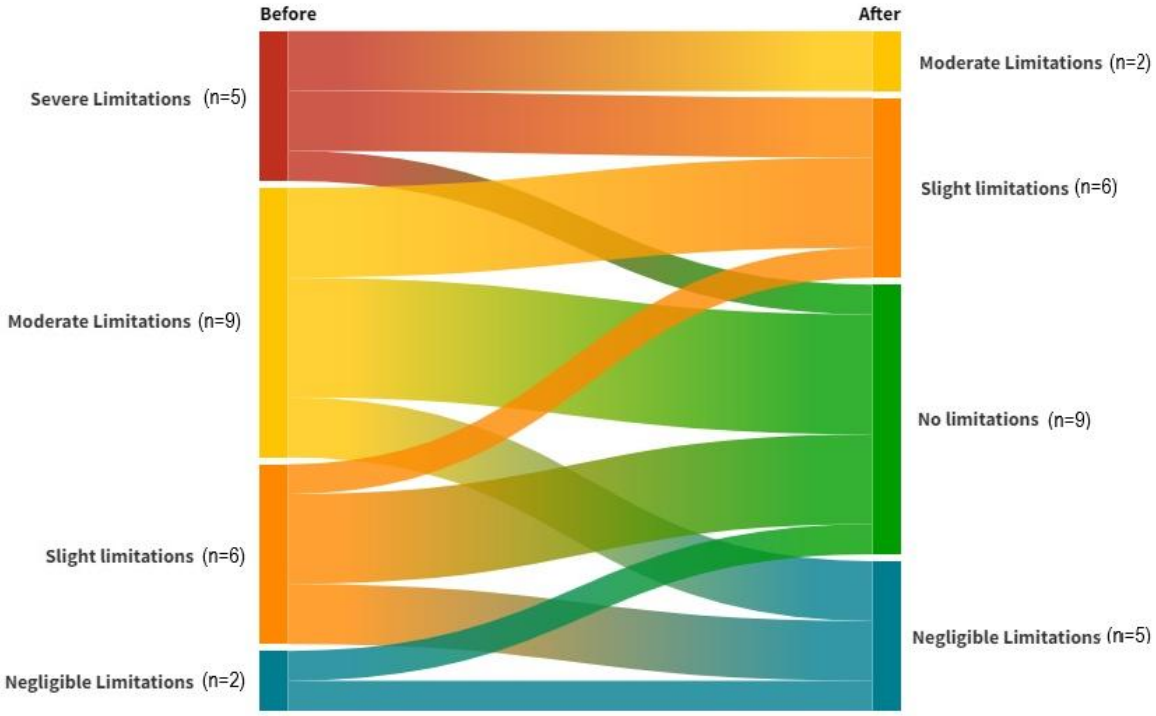

Figure 3. Comparison of PCFS pre and post intervention.

Discussion

This study compared the effects, feasibility, adherence, and adverse events of a supervised high intensity endurance and strength training plus multimodal home-based exercise programs on physical and functional outcomes in individuals after hospitalization due to COVID-19. Although adherence was decreasing over time, the exercise program demonstrated improvements in exercise capacity, functionality, muscle strength, pulmonary function, quality of life, and symptoms of anxiety and depression among post-hospitalized patients with COVID-19. Notably, no adverse events were reported. The combination of supervised outpatient training and home-based exercises provided a comprehensive approach to physical fitness and rehabilitation, statistically significant improvements in important clinical variables in post-hospitalized patients with COVID-19.

The consequences of prolonged immobilization in intensive care units (ICU) were noted with influence on the impairment of pulmonary and multisystemic function, consequently impacting on the demand for rehabilitation of these patients, in a study by Aul et al. (19) on post-hospitalized COVID-19 patients, those who were intubated and had persistent respiratory symptoms presented more risk of developing post-COVID pulmonary fibrosis characterized by poor lung function.The study by Ong et al. (20) investigated the association between lung function and exercise capacity, showing that mild residual lung function sequelae were detected in over half of the recovered patients three months after hospital discharge and 41% had negatively affected the exercise capacity. Although previous study on patients with other lung diseases have demonstrated the benefits of pulmonary rehabilitation in improving exercise tolerance, dyspnea symptoms, and quality of life (21), however, there is a lack of specific research on the benefits of exercise programs on pulmonary function and exercise capacity in individuals with COVID-19. In our study, individuals exhibited an improvement in pulmonary function and exercise tolerance after intervention. This finding aligns with prior research conducted in this field. Among the limited number of clinical trials in this area, Liu et al. (2020) demonstrated enhancements in forced expiratory volume and forced vital capacity (22). Conversely, Cursi et al. (2020), reported improvement in exercise capacity (23). However, the study involved a cross sectional design, therefore their findings and associations are limited.

Previous studies demonstrated the positive impact of physical exercise on the recovery of hospitalized patients with COVID-19. These studies have highlighted improvements in various aspects such as muscle strength, pulmonary function, muscle mass, and aerobic capacity in individuals after COVID-19 (6,23). Unlike previous investigations, our study sought to examine the potential benefits of a combined approach involving supervised high intensity exercises and multimodal home-based training on an extensive evaluation of functional tests and questionnaires in patients with COVID-19. Furthermore, we incorporated physical and physiological variables, as assessed in the study by Silva et al (6), where individuals in the telerehabilitation intervention group showed improvements in outcomes related to functional capacity, including the 6-minute step test,2-minute stationary walk test, sit-to-stand test (30 second), and quality of life assessment (SF-36), in individuals after COVID-19 hospital discharge.

To our knowledge, there is limited literature reporting on the effectiveness of such a multimodal program in addressing these specific outcomes in this population. A previous study did not report benefits of multimodal exercise combined with exercise at home on psychological symptoms and functionality in patients with COVID-19 (22). One possible explanation for the observed improvements across all physical and physiological variables in our study could be the duration of our intervention. According to the literature, duration of the exercise program is important since exercise does not provide an overall level of beneficial effect until the completion of at least 8-weeks of continuous training (24). Most programs described in the literature were between 2 to 6 weeks, which is considerably shorter than the duration implemented in our program (14 weeks), as observed in the rehabilitation program by Asimakos et al. (25), with an 8-week intervention duration, investigated the effects on respiratory symptoms, fatigue, functional capacity, mental health and health-related quality of life in patients with COVID-19 pneumonia, 6-8 weeks posthospital discharge. By extending the duration of the intervention, we may have provided patients with a more substantial and prolonged period for complete functional recovery. In addition, incorporating supervised rehabilitation sessions and a structured exercise regimen for home-based training, our program could optimize the potential benefits derived from exercise interventions. For this reason, as a clinical message, this rehabilitation our program would be recommended in post-hospitalized patients with long COVID.

Regarding the training intensity adopted in our study, it was observed that the type of training could have favorable effects that resulted in positive outcomes in just eight weeks, confirming the findings of a comparative study on low-intensity and high-intensity cardiopulmonary rehabilitation programs in patients with the same epidemiological profile, but with a longer duration of at least three months. In this longer-duration study by Dumitrescu et al. (26), it was demonstrated that low-intensity exercises can expedite quicker recovery and improve overall fitness to similar levels as the high-intensity group. According to Jimeno-Almazán et al., a supervised, tailored concurrent training program at low and moderate intensity for both resistance and endurance training is a more effective, safe, and well-tolerated intervention in post-COVID-19 conditions (27).

Related to psychological state, in the study by Oliva et al. (28) no significant differences were found at anxiety levels after pulmonary rehabilitation intervention, which contrasts with the findings of our study, where anxiety had a notable impact on reducing anxiety levels, but it did not produce the same effect on depression levels. This indicates that the changes in anxiety and depression levels follow the same pattern in response to the intervention, an improvement was observed, but it was not statistically significant, In the rehabilitation program by Asimakos et al. (25), when depression was assessed using HADS, no statistically significant difference was observed. However, when assessed using the Beck Depression Inventory (BDI), it showed greater specificity in this variable, indicating it to be a more precise instrument (29). Given this, as seen in other research, there is a high prevalence of psychiatric and cognitive impairments following SARS-CoV-2 infection, specifically common mental disorders, depression, and anxiety (30).

Finally, our study has some limitations. First, this is a nonrandomized control study, without a control group. Our study was conducted during the pandemic period in hospital, and in the literature, at that time, there were few randomized controlled trials conducted due to recruitment difficulties caused by social distancing and government restrictions. However, we have proposed a new intervention which is feasibility, with good adherence, and without adverse events associated. Furthermore, in comparison with previous studies, we have analyzed the effect of our structured rehabilitation program on several physical and physiological variables. Future randomized controlled studies are necessary in this field, to know the best rehabilitation protocol, and to be able to establish a specific program design for the rehabilitation of patients with COVID-19

Conclusion

In conclusion, the present study demonstrates that there was improvement in most evaluated outcomes following 8-week face-to-face high intensity rehabilitation program and a structured exercise regimen for home-based training, enhancing exercise functional capacity, muscle strength, symptoms of anxiety, and functional status in post-hospitalized COVID-19 patients, demonstrated to be feasible and safe.

Conflicts Of Interest

The authors declare no conflict of interest.

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