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Effects of cardiopulmonary and metabolic rehabilitation in post-COVID-19 patients: Clinical trial

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Abstract

Objective: To evaluate the effects of cardiopulmonary rehabilitation on the functional capacity of post-COVID-19 individuals.

Methods: Clinical trial, 7 patients participated in the study who tested positive for COVID-19. Participants underwent a 30-session rehabilitation program. They were evaluated using: Post COVID-19 Functional Scale (PCFS), inspiratory and expiratory muscle strength, 6-minute walk test (6MWT), 30-second sit-to-stand test (SE30'), hand grip (HG), VO2max, maximum HR, resting and reserve. Functional variables were analyzed using ANOVA for repeated measures and the Bonferroni multiple comparison test, considering a significance level of 5%.

Results: The participants showed improvement in their functional status, with a decrease in the PCFS score (p=0.006), improvement in MIP (p=0.013), distance covered in the 6MWT (p=0.022), HGSR (p=0.005) and HGSL (p=0.009). In SE30', they showed improvement in the intermediate (p=0.002) and final (p=0.046) assessments.

Conclusions: The individuals demonstrated a decrease in functional limitations, improvement in functional capacity, inspiratory and lower limb muscle strength, handgrip strength after the 7th week of rehabilitation, with maintenance of the functional status being promoted until the end of the program. Implying the reestablishment of the global functional state of the pa-tients.

Keywords: Rehabilitation; Acute COVID-19 syndrome; Functional status; Physical therapy specialty.

Introduction

The new coronavirus, SARS-CoV-2, emerged in December 2019, SARS-CoV-2, expanded throughout China, soon after reaching worldwide proportions [1,2]. It is a virus with high transmissibility [3,4] and an estimated mortality rate of approximately 3.7% [3,5].

Most COVID-19 infections are mild, but they can be severe or critical, causing dyspnea, hypoxemia, severe lung damage, respiratory failure, septic shock, and multiple organ failure [6-8], requiring oxygen supplementary and prolonged mechanical ventila-tion [9]. The presence of comorbidities such as Chronic Obstructive Pulmonary Disease (COPD), asthma, heart disease, cerebrovascular disease, diabetes, kidney failure and cancer are associated with a worse prognosis and longer hospital stay [10,11].

People who need prolonged hospitalization are more susceptible to developing muscle weakness acquired in the ICU [12,13], loss of muscle function and decreased functional capacity [14], diaphragmatic muscle weakness, decreased lung compliance [15,16], developing the critically ill polyneuromyopathy syndrome (CDP) [17], impacting on the decrease in quality of life [18].

Complications arising from COVID-19 in the lung tissue such as fibrosis, consolidation, vascular thickening, pleural effusion, bronchiectasis can occur in most patients [15]. These seem to be prone to movement-related fatigue, similar to patients with ARDS, even those who do not develop critical illness [17].

Previous studies have shown that post-COVID-19 rehabilitation, involving aerobic and resistance exercises, combined with respiratory muscle training, is able to improve functional capacity [19], peripheral muscle strength [20], respiratory function and quality of life [21] in individuals affected by the disease. Therefore, rehabilitation following SARS-CoV-2 infection is an essential component of the care plan for this population [22].

However, there is a lack of evidence regarding outpatient rehabilitation after COVID-19. Thus, the present study aimed to evalu-ate the effects of cardiopulmonary and metabolic rehabilitation on the functional capacity of post-COVID-19 individuals.

Materials and methods

This is a clinical trial, in which a sample of individuals after infection with the SARS-CoV-2 virus was included. To participate in the study, individuals should be over 18 years of age, of both sexes, and present a positive RT-PCR or RT (rapid test) for COVID-19 in the last 4 months prior to inclusion (Figure 1). Participants were referred by partner health services. We considered the following exclusion criteria, patients who did not have a positive RT-PCR or TR, those with positive tests in a period longer than four months of inclusion, individuals with hemodynamic instability, physical limitations that prevented the performance of the initial evaluations, accident cerebrovascular disease, cancer and previous myocarditis. The present study was approved by the Ethics and Research Committee (CAAE 42014621.7.0000.5333) and the participants signed the informed consent form (TCLE).

The sample comprised 7 individuals (Table 1), who underwent a cardiopulmonary and metabolic rehabilitation program con-sisting of 30 sessions. The participants were submitted to a complete functional evaluation in 3 moments: Pre-participation, after 15 sessions and at the end of the program.

The assessment consisted of the Post-COVID-19 Functional Status Scale (PCFS), developed to monitor the course of symptoms and their impact on the functionality of patients infected with COVID-19 after hospital discharge. It has 6 levels: 0(no functional limitations), 1(insignificant functional limitations), 2(mild functional limitations), 3(moderate functional limitations), 4(severe functional limitations) and D(death). The scale was applied by a physiotherapist at baseline, intermediate and final assessments [23].

Functional capacity was measured by the six-minute walk test (6MWT). Performed in a corridor free of people, participants were instructed to walk at a fast pace for 6 minutes along a 30-meter course. Blood Pressure (BP), Heart Rate (HR), Oxygen Saturation (SpO_2) and subjective effort scale for tiredness and dyspnea (modified BORG) were measured before and after the test. At the end of the test, the distance covered by the individual was checked and placed in the formula, which takes height, age and body weight into account, obtaining the normality parameter for each case [24].

Respiratory muscle strength, Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) were assessed using a digital manovacuometer (MVD 300-U Homed). Both pressures were measured three times, obtaining a difference less than or equal to 10% between the 3 repetitions, interspersed with 2 minutes of rest, the highest value being considered. Between MIP and MEP measurements, there was a five-minute interval [25].

For Handgrip Strength (HGS), a handheld hydraulic dynamometer (Saehan-5001) was used. The test was performed with the individual sitting on a chair, with shoulders adducted, neutral rotation and elbow flexion at 90°, forearm in a neutral position holding the dynamometer and arm parallel to the body. From this position, the individuals were instructed to perform a maximum contraction during expiration. Three consecutive tests were performed and the average used as the HGS value. The test was performed on both limbs [26].

Indirect maximal oxygen consumption (VO2max) was measured using the Exercise Test (ET) on a treadmill (Inbrasport model ergometer) with a 12-lead electrocardiogram (Inbramed), using the Naughton protocol. The protocol starts with a treadmill speed of 1.0 miles per hour (mph) without incline, for warm-up purposes. Then go to 2.0 mph, maintaining zero elevation. From this stage, the speed is fixed at 2 mph and the ramp elevation is incremented by 3.5% every 3 minutes. HR, BP, $SatO_2$, Borg pre and post test were evaluated [27].

The sessions were held at the Cardiopulmonary and Metabolic Rehabilitation Center of the Institute of Cardiology/University Foundation of Cardiology (IC/FUC). Duration of 15 weeks, 2 sessions per week of 60 minutes each, totaling 30 sessions. HR, SpO_2, BP and BORG were monitored in all sessions.

The rehabilitation protocol consisted of warm-up, respiratory muscle training, aerobic training, resistance training and stretching. The warm-up took place at the beginning of each session (stationary gait, shoulder flexion and extension, shoulder circumduction, trunk rotation, plantiflexion in orthostasis), consisting of 30 quick repetitions of each exercise.

Inspiratory Muscle Training (IMT) was performed shortly after warm-up. The POWERbreathe® inspiratory training device (POWERbreathe International Ltd., England, United Kingdom) was used. It consisted of five series of ten repetitions each, with a one-minute rest between each series. During training, patients were instructed to maintain diaphragmatic breathing. Subjects were submitted to IMT of moderate to high intensity, with an initial load set at 50% of MIP during the first two weeks, allowing for an adaptation period. Sequentially, load increases occurred at 55% MIP week 3, 60% MIP week 4, 65% MIP week 5, MIP 70% week 6, MIP 75% week 7, and MIP 80% of MIP in the 8th week. From weeks 9 to 15, load was adjusted weekly to maintain 80% MIP [28].

Aerobic training consisted of walking on a treadmill for 30 minutes, with a workload adjusted between 60%-80% of the maximum heart rate obtained through the exercise test.

Resistance muscle training consisted of 2 workouts: Workout A (extension/push exercises: diagonal abduction, machine bench press, rope triceps, leg extension, unilateral knee flexion, horizontal leg press and plantiflexion on the machine) and B (exercises of "pulling"/flexion: front pull, machine biceps, diagonal adduction, hip extension, squat, orthostasis plantiflexion and extension chair). All exercises were performed in 3 series of 10 repetitions and the load was adjusted weekly aiming at muscle fatigue in the last 3 repetitions.

At the end of each session, participants performed static stretching of lower and upper limbs, sustained for 30 seconds.

Statistical analysis

Data are presented as mean and standard deviation, and absolute frequency and percentage. For the analysis of the functional variables, the analysis for repeated measures (ANOVA) and the Bonferroni multiple comparison test were used. A significance level of 5% was used. The Statistical Package for the Social Sciences (SPSS) Windows v.22.0 program was used.

Considering an α=5% error and a power of 80%, the sample was calculated for 44 subjects, based on a previous study [34], tak-ing into account 10% of possible losses. The sample calculation was performed using the Winpepi program.

Results

Persistent post-COVID-19 sequelae at the time of assessment are described in Table 2. The results of the analyzed variables are shown in Table 3. Patients showed significant improvement in PCFS, when comparing baseline and final assessments. In the assessment of respiratory muscle strength, there was an improvement in MIP and MIP% from baseline to the intermediate as-sessment (7^{th} week) and the mean was maintained after the final assessment (15 weeks). There were no differences in MEP and PE%.

In the measures of submaximal functional capacity evaluated by the 6MWT, the patients presented a greater distance covered and a higher percentage of the predicted distance when comparing the baseline and intermediate evaluations, with maintenance of the average values in the final evaluation, however, there was no difference for BORG fatigue and BORG dyspnoea.

The participants showed a significant improvement in lower limb strength, assessed by the 30' sit-to-stand test, and handgrip strength in both limbs, when baseline and intermediate assessments were compared. In both tests, mean values were maintained at the time of the final evaluation. No difference was observed in any of the variables evaluated by the exercise test.

Discussion

Our results demonstrate that individuals who underwent a cardiopulmonary and metabolic training program after COVID-19 infection improved their functional limitations, inspiratory muscle strength, lower limb muscle strength, and handgrip strength. However, this improvement was noticed in the intermediate evaluation and was not maintained until the final evaluation.

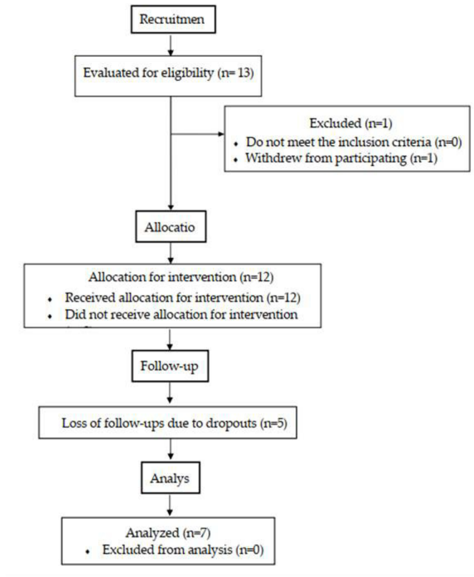

Figure 1: Study flow chart.

Table 1: Sample characteristics.

Variable	N = 7 (%)
Age (years)	53,2 ± 16,1*
Sex	
Feminine	3 (42,8)
Masculine	4 (57,1)
Mass (kg)	75,6 ± 15,9*
Height (cm)	162,4 ± 11,4*
BMI (kg/m²)	28,4 ± 3,7*
Comorbidities	
DM	2 (28,6)
Obesity	3 (42,8)
SAH	3 (42,8)
Dyslipidemia	2 (28,6)
Sedentary lifestyle	5 (71,4)
Ischemic heart disease	1 (14,3)
Hypothyroidism	1 (14,3)
Hospitalization	
Need for hospitalization	5 (71,4)
Hospitalization days	14,7 ± 12,1*
Ventilatory support	3 (42,8)
NC	3 (42,8)
NRRM	1 (14,3)
HFNC	1 (14,3)
NIV	0
IMV	2 (28,6)
Medicines	
Antihypertensive	3 (42,8)
Anticoagulant	1 (14,3)

*M±DP: Mean And Standard Deviation. BMI: Body Mass Index; DM: Diabetes Mellitus; SAH: Systemic Arterial Hypertension; NC: Nasal Catheter; NRRM: Non-Rebreathing Reservoir Mask; HFNC: High-Flow Nasal Catheter; NIV: Non-Invasive Ventilation; IMV: Invasive Mechanical Ventilation.

Table 2: Post-COVID-19 sequelae.

Sequelae	N = 7 (%)
Fatigue/tiredness	5 (71,4)
Dyspnea	1 (14,3)
Headache	0
Muscle pain	1 (14,3)
Loss of hair	3 (42,8)
Taste/smell loss	3 (42,8)
Chest pain	1 (14,3)
Dizziness	0
Cough	2 (28,6)
Palpitations	0
Cepression/anxiety	6 (85,7)
Difficulty with reasoning, language and memory	3 (42,8)

When applying the PCFS, we observed that our sample consisted of patients who went through different stages of disease severity. Hussein et al. [29], demonstrated that patients recovered from COVID-19 obtained fluctuating degrees of restrictions in their work-related, public and leisure activities or activities of daily living. Despite the heterogeneity and sample size, our study showed a significant improvement in the degree of functionality of patients recovered from COVID-19 who participated in a cardiopulmonary and metabolic rehabilitation program, starting from a mild to moderate degree of functionality to insignificant. Pant et al. [30], point out that the consequences on physical and mental health in post-COVID-19 patients need to be observed and that rehabilitation measures in post-acute care are essential.

Our findings are in line with the findings of Ahmed et al, who, through a pulmonary function test, demonstrated that the inspiratory muscle training performed obtained a significant improvement in the values of FVC% and FEV1%. In this study, the patients performed 2 daily sessions, 5 days a week, for 2 consecutive weeks with a threshold load of 50% of the maximum inspiratory pressure (MIP) [31]. In our study, we used a threshold of up to 85% of MIP using 5 sets with 10 repetitions and 60 seconds of rest between sets. The results in the inspiratory muscle training, mainly up to the 7th week, showed a significant increase, also reflecting in the improvement of the quality of life and functional capacity.

Kai Liu et al. [21] conducted a study with respiratory rehabilitation in post-COVID-19 patients for 6 weeks, 2 sessions per week and once a day for 10 minutes (at home). The authors observed that in the intervention group there was a significant improvement in the 6MWT distance and in the pulmonary function test. These findings corroborate ours and are compatible with the weeks of rehabilitation in which we obtained important differences in the global functional status. We can deduce that a smaller number of sessions combined with inspiratory muscle training is able to increase the functional capacity of patients recovered from COVID-19.

Despite the significant increase in the distance covered in the 6MWT, there was no difference in maximum VO2, maximum HR, reserve HR and resting HR. However, as shown in Table 3, we observed important clinical differences at all moments of maxi-mum VO2 evaluation. The non-difference can be explained by the low sample number.

Table 3: Functional variables.

	Assessment moments			
	First	Intermediate	last	p value
PCFS	1,9 ± 0,7	0,9 ± 0,7	0,6 ± 0,8	0,006†
Pimáx	85,6 ± 31,2	113,4 ± 27,5	113,3 ± 40,9	0,013*
PI%	83,6 ± 31,2	112,9 ± 18,9	113,3 ± 40,9	0,015*
PEmáx	104,6 ± 44,1	127,4 ± 38,6	108,5 ± 31,3	0,227
PE%	100,0 ± 32,4	122,2 ± 31,1	105,8 ± 31,4	0,231
6MWT				
Dist(m)	464,1 ± 57,5	539 ± 22,4	513,7 ± 40,6	0,022*
%pred	86,1 ± 18,7	99,8 ± 15,2	95,7 ± 15,4	0,027*
BORGFpré	0,3 ± 0,7	0	0	0,397
BORGFpós	1,6 ± 3	0,2 ± 0,4	0,1 ± 0,2	0,207
BORGDpré	1,4 ± 2,9	0,07 ± 0,2	0	0,246
BORGDpós	1,1 ± 1,7	0,1 ± 0,2	0	0,099
SE30' (rep)	10,2 ± 0,9	12,6 ± 0,8	12,1 ± 1,8	0,002*†
RHGS(kgf)	27,3 ± 9,5	32,6 ± 7,7	32,9 ± 8,6	0,005*
LHGS(kgf)	24,5 ± 9,9	31,2 ± 8,2	30,6 ± 8,7	0,009*
ET				
VO2max	32,2 ± 7,7	40,3 ± 4,9	38 ± 10,5	0,109
HRmax	135,7 ± 27,2	146,7 ± 25,9	135,6 ± 33,8	0,102
HRre	73,6 ± 15,6	68,9 ± 9,5	72 ± 21,8	0,701
HRres	67,6 ± 26,8	77,9 ± 21	63,6 ± 21,4	0,075

*: statistically significant between baseline and intermediate assessment, for p < 0.05. †: statistically significant between baseline and final assessment, for p<0.05. Values are expressed as mean±SD. PCFS The Post COVID-19 functional status; PImax: maximum inspiratory pressure; PI%: % of predicted maximum inspiratory pressure; PEmax: maximum expiratory pressure; PE%: % of predicted maximum expiratory pressure; 6MWT: 6-minute walk test; Dist: distance from the 6MWT; BORGF: BORG scale muscle fatigue; BORGD: BORG scale dyspnea; SE30': 30-second sit and stand test; RHGS: right hand grip strength; LHGS: left hand grip strength; ET: exercise test; VO2max: maximum oxygen volume; HRmax: maximum heart rate; HRre: resting heart rate; HRres: heart rate reserve. Significance level of p<0.05.

Silva et al. [32] demonstrated that lower limb strength and aerobic resistance are associated with the practice of regular physical exercise, which is related to better performance in the sit-to-stand test and the 6MWT. In line with these findings, our study found that there was an improvement in performance when performing the sit-to-stand test at all times evaluated.

Del Brutto et al. [33] showed in their study a greater than 5% loss of handgrip strength after coronavirus infection, while Sansin et al [34] observed decreased handgrip strength in patients who required hospitalization, mainly among women. Results which suggest the musculoskeletal damage generated by SARS-CoV-2. Our program resulted in increases in handgrip strength by up to 27%, thus indicating improved overall muscle strength.

Even with limitations such as low adherence to cardiopulmonary and metabolic rehabilitation, the number of patients who completed the program, the difficulty in recruiting patients to participate in the study and our rehabilitation center is not a reference for the treatment of COVID-19, our study was able to demonstrate that a program with a reduced number of sessions is safe and effective.

Therefore, we showed that a rehabilitation program for post-COVID-19 patients was able to provide functional improvements in these individuals from the 7th week onwards, with 15 sessions performed. We suggest that shorter duration programs be adopted aiming at greater adherence and segment of these patients. Given the brevity of the onset of the disease, more robust studies are needed to delve deeper into the effects of rehabilitation in this population.

Conclusion

Individuals post-COVID-19 infection, submitted to a 15-week rehabilitation program, demonstrated improvement in functional limitations after the end of the program. They showed improvement in functional capacity, inspiratory muscle strength, lower limb muscle strength and handgrip strength after the 7th week of treatment, maintaining the functional state until the end of the proposed program. Due to the large number of dropouts during follow-up, we believe that a program of 15 sessions lasting 7 weeks is sufficient for the functional recovery of these patients.

Declarations

Funding: This research received no external funding.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of interest: The authors declare no conflict of interest.

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