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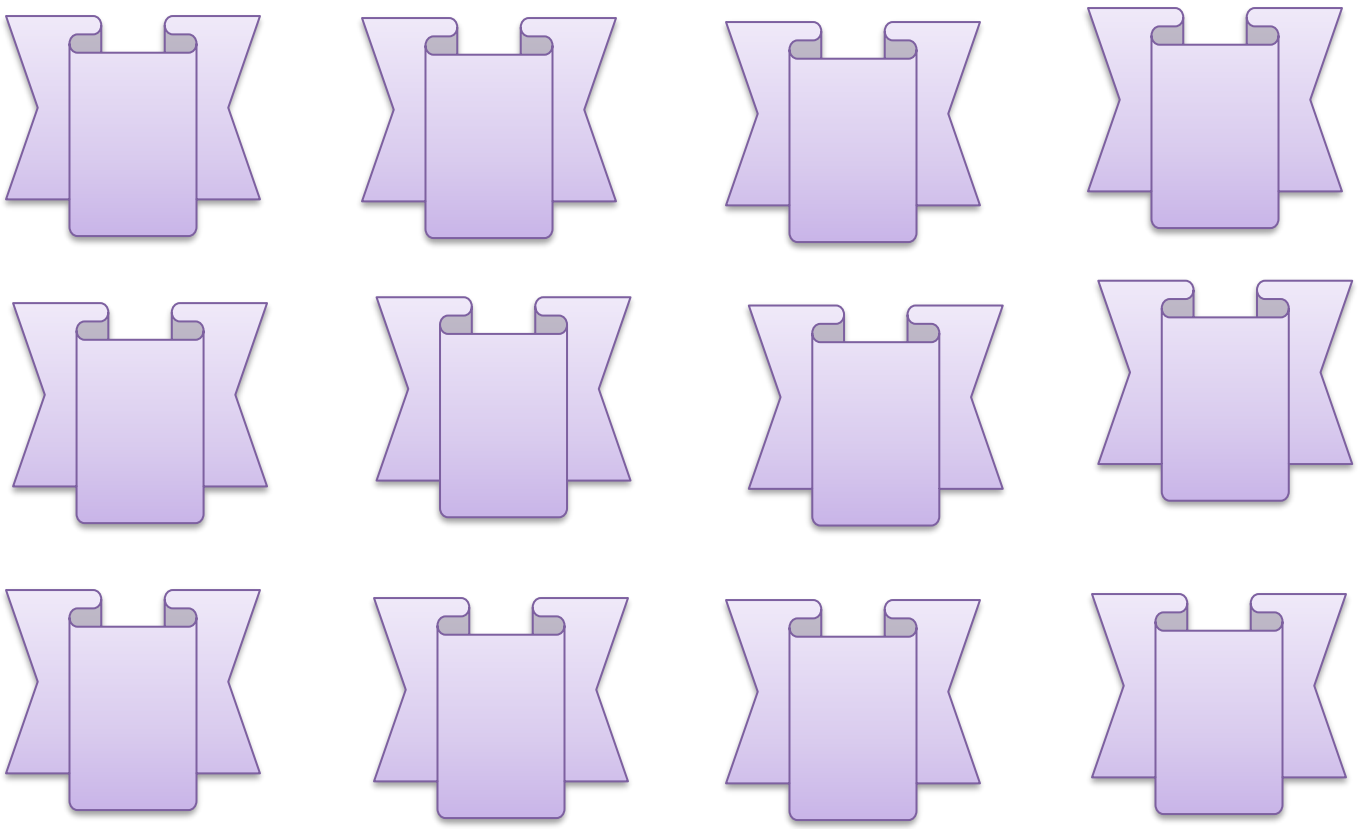

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Original Article

Effect of Combined Exercise Training on Functional Capacity in Post Covid-19 Pulmonary Fibrosis

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ABSTRACT

Background: Post COVID-19 pulmonary fibrosis is considered as one of the most long-term pulmonary complication of Coronavirus Disease [COVID-19], being an infectious respiratory condition, which characterized by progressive exertional dyspnea, fatigue, reduced exercise capacity and health related quality of life.

The Aim of the work: This study aimed to determine the effect of combined exercise training on functional capacity in post COVID-19 pulmonary fibrosis.

Patients and Methods: Forty patients of both sexes with Post COVID-19 pulmonary fibrosis with an age above 25 years old. They were recruited from the outpatient clinic at Al-Mamora chest hospital. Patients were assigned into two group; Group A [study group] which received 8 weeks [3 sessions per week] of combined exercise training [consisting of aerobic, resisted training] and breathing exercises along with the pharmacological treatment and Group B [control group] which received 8 weeks [3 sessions per week] of breathing exercise along with the pharmacological treatment. after thorough assessment of functional capacity through [6MWT], dyspnea during activity by mMRC, and measure Pulmonary function test [FVC].

Results: There was statistically significant [P<0.001] decrease of the mean values of mMRC dyspnea scale, a statistically significant [P<0.05] increase of the mean value of 6MWT after management that were significantly higher in group A associated with a non-statistical change [p-value >0.05] in the mean value of FVC. There were significant improvements in all outcomes [P-value<0.05] after management that were significantly higher in group A except the pulmonary function test [FVC] was a non-significant improvement [p-value >0.05].

Conclusion: Eight weeks of combined exercise training improves functional capacity decreasing patients' physical and functional disabilities, promoting a much more independent and functional lifestyle.

Keywords: COVID-19; Pulmonary fibrosis; Functional capacity; Combined exercise training.

INTRODUCTION

Coronavirus Disease [COVID-19] is an infectious respiratory illness that spreads quickly from person to person and is caused by a virus known as severe acute respiratory syndrome virus 2 [SARS-CoV-2] it can cause a wide range of clinical symptoms, from no symptoms such as light flu to pneumonia causing acute respiratory failure or severe acute respiratory distress syndrome necessitating admission to the intensive care unit[ICU] and possibly even death. While the majority of COVID-19 patients do make a full recovery, over 70% still have systemic attachments four months following diagnosis known as Long-term COVID-19 complications. One of the lung problems produced by this illness is Pulmonary fibrosis [1]. Patients in the third stage of COVID-19 often develop pulmonary fibrosis [PF] [2].

Pulmonary fibrosis is a lung disorder characterized by several manifestations of a multisystem disease including different persisting symptoms mainly pulmonary, including dyspnea on exertion, dry cough, muscle aches, chest pain, decreased exercise capacity, fatigue, and in severe cases, the requirement for oxygen supplementation [3].

Pulmonary fibrosis with decreased functional capacity means a dimension of an individual's overall capability to perform specific activities, including mobility, communication, self-care, self-direction, work tolerance, and work skills. These factors are categorized based on qualifiers from the International Classification of Functioning, Disability and Health [ICF] related to assessments like the six-minute walk test [6MWT] and the St George Respiratory Questionnaire [SGRQ] [4].

There isn't a well-established therapeutic approach for treating post COVID -19 fibrosis. pharmacological treatments and pulmonary rehabilitation [PR] could be taken into consideration, though, as a post-COVID-19 fibrosis patient's supplemented oxygen need during exercise was found to benefit from a 10-session exercise-based PR program that included aerobic, resisted, and stretching exercises [1].

Several studies have shown that pulmonary rehabilitation may be helpful for post-COVID fibrotic lung disorders, in addition to pharmacologic therapy. There have been no reports of recommendations or comprehensive evaluations of pulmonary rehabilitation after acute COVID-19. The treatment recommendations of COPD and other chronic pulmonary disorders, such as interstitial lung disease, were the basis for a pulmonary rehabilitation program that was proposed in many narrative reviews [ILD] [5]. Pulmonary rehabilitation doesn't cure and cannot reverse the anatomical alterations; however, it does reduce dyspnea and enhance functional capacity, muscle strength, functional capacity, mobility and quality of life in post COVID-19 pulmonary fibrosis patients [6].

Exercise training, a core component of pulmonary rehabilitation in ILD, and many observational studies have shown that patients with ILD who undergo this program have improvements in their functional ability, dyspnea, and HRQoL. These changes are statistically and clinically significant [7].

It is advised to engage in aerobic exercises for 3 to 5 days per week, with each session lasting 20 to 30 minutes. The intensity and duration of these exercises should be adjusted based on the patient's individual tolerance. For the development of peripheral muscles, a progressive resistance training program is recommended, focusing on both upper and lower muscle groups. This training should be performed 2 to 3 times per week, with 8 to 12 repetitions being the maximum for each exercise. Rest intervals of 2 minutes should be taken between one to three sets of repetitions. The patients undergoing recovery from Covid-19 benefited from a respiratory rehabilitation program that included pursed lip breathing and diaphragmatic breathing. It resulted in an improvement in their quality of life [QOL]. Additionally, it is anticipated that there will be a weekly strength improvement of around 5 to 10% [8, 9].

When it comes to ILDs, in terms of health-related quality of life, hypoxemia is a common occurrence for this patient. During the day, its main symptoms include decreased energy and worse physical and social performance. Supplemental oxygen treatment is likely to alleviate symptoms and enhance quality of life for patients who have resting hypoxemia or significant oxygen desaturation during exercise. This is why oxygen therapy is so important for treating pulmonary fibrosis, especially pulmonary fibrosis after COVID-19 [10].

This study aimed to determine the effect of combined exercise training on functional capacity in post COVID -19 pulmonary fibrosis.

PATIENTS AND METHODS

This study followed the principles outlined in the "Declaration of Helsinki" and was conducted as a randomized controlled trial. Before actively participating in the study, all patients provided written informed consent after receiving a comprehensive explanation of the study's objectives and procedures. Additionally, the research ethical committee of the faculty of physical therapy at Cairo University approved the study under the code number No.P.T.REC/012/004911.

Sample and randomization

Sample: Forty patients [31men and 9 women] with Post COVID-19 pulmonary fibrosis with ages above 25 years old and BMI of 18.4-42.7 kg/m2 were recruited from the outpatient clinic at Al-Mamora chest hospital and had positive CT chest findings fibrotic abnormalities of post COVID-19 or had acute respiratory distress syndrome survivors related to COVID-19 leading to their intensive care unit [ICU] admission and treatment.

Randomization: The eligible patients were randomly assigned using closed envelop method into: two equal group in number; Group A: [n=20] patients received combined exercise training [consisting of aerobic, resisted and breathing exercises], and Group B: [n=20] patients received breathing exercise along with the pharmacological treatment.

Evaluation procedures: All patients were evaluated before and after 8 weeks of the management using the following measures; Six-minute walk test [6MWT], Modified Medical Research Council dyspnea scale [mMRC dyspnea scale], and Pulmonary function test [FVC] [11, 12].

Therapeutic intervention

Aerobic exercises [Walking on a treadmill]: Treadmill was used to perform aerobic exercise with intensity of training starting as 70–80% of the maximum speed achieved during a six-minute walking test [6MWT] and targeted to reach 80–90% of individual average walking Speed during a six-minute walking test [6MWT] but modified according to patient's tolerance and Borg scale. Duration of each session was 20-30 minutes with 2 minutes of exercise alternating with 2 minutes of rest for 3 sessions/week for 8 weeks [8]. Patients on LTOT applied exercise under oxygen administration in order to maintain a SpO2 of at least 90 %used nasal cannula or oxygen mask with 20L flow of O2 per minute [12].

Resisted training: The major muscle groups exercise trained were shoulder press muscles, leg press muscles, chest press muscles and supported one leg step up exercise [quadriceps, hamstring and gluteal muscles], upper limb exercise started with intensity of 30 – 40 % of RM and lower limb exercise with 40 – 50 %repetition maximum [RM]. intensity increased from rate of percervid exertion [RPE] of 3to 5 [without pain] representing 30 to 50% of 1RM to 4 to 6 RPE representing 60 to 80% of 1RM while maintain a SpO2 of more than 90% this performed for 3 sessions/week, 3 sets per exercise with 10–15 repetitions per set with a 2-min rest between sets, and lasted 30 min[13].

Breathing exercise: Breathing exercise consisted of Pursed-lip breathing and Diaphragmatic breathing exercises were patients performed 3 sets of 5 repetitions per set for each breathing exercise with 2 min rest in between lasted for 15 minutes and progressed by holding inhalation [14].

Exclusion criteria: Patients were excluded if they had; acute respiratory acidosis on arterial blood gases [ABG], a medical history of conditions like cancer, spinal cord disease, or neuromuscular diseases that could potentially impact their functional capacity, muscle strength, and quality of life, any previous lung surgery, cognitive impairments, pregnant women, patients with a previous history of interstitial lung disease [ILD] and cardiovascular co-morbidities [recent myocardial infarction, acute heart failure, severe mitral stenosis].

Statistical analysis: The data analysis was performed using the statistical package for social sciences, version 23.0 [SPSS Inc., Chicago, Illinois, USA]. For quantitative data that followed a normal distribution, the mean ± standard deviation and ranges were used for presentation. Non-normally distributed variables [non-parametric data] were presented as the median with inter-quartile range [IQR]. Qualitative variables were presented as numbers and percentages. To assess normality, the Kolmogorov-Smirnov and Shapiro-Wilk tests were used. Within-group comparisons of

outcomes before and after management were conducted using the paired t-test. A p-value of less than 0.05 was considered statistically significant. To detect differences in demographics [excluding sex] and outcomes between groups, an independent t-test was performed. The distribution of sex was analyzed using the chi-squared test and Fisher's exact test.

RESULTS

Forty post COVID-19 pulmonary fibrosis [31 men and 9 women] were included in this study. One patient didn't complete the study [was die]. So, data was analyzed for 39 patients [20 in study group and 19 in control group] who complete all assessment and management.

Demographics: There was no significant difference between group in age, height, weight and BMI of the patients [p>0.05] as seen in Table [1].

Effect of combined exercise training [consisting of aerobic, resisted and breathing exercises] on 6MWT, mMRC and Pulmonary function test [FVC] in both groups

Within group comparison: Pre and post management mean values of 6MWT, mMRC and PFT [FVC] in both groups were presented in table [2]. There was significant improvement in 6MWT, mMRC post- management in both groups [p<0.0001]. There was no significant difference between groups [study and control] before treatment [p>0.05]. There was non-significant improvement in PFT [FVC]. When comparing the two groups after eight weeks of management there was significance difference [p≤0.001] in support of group A.

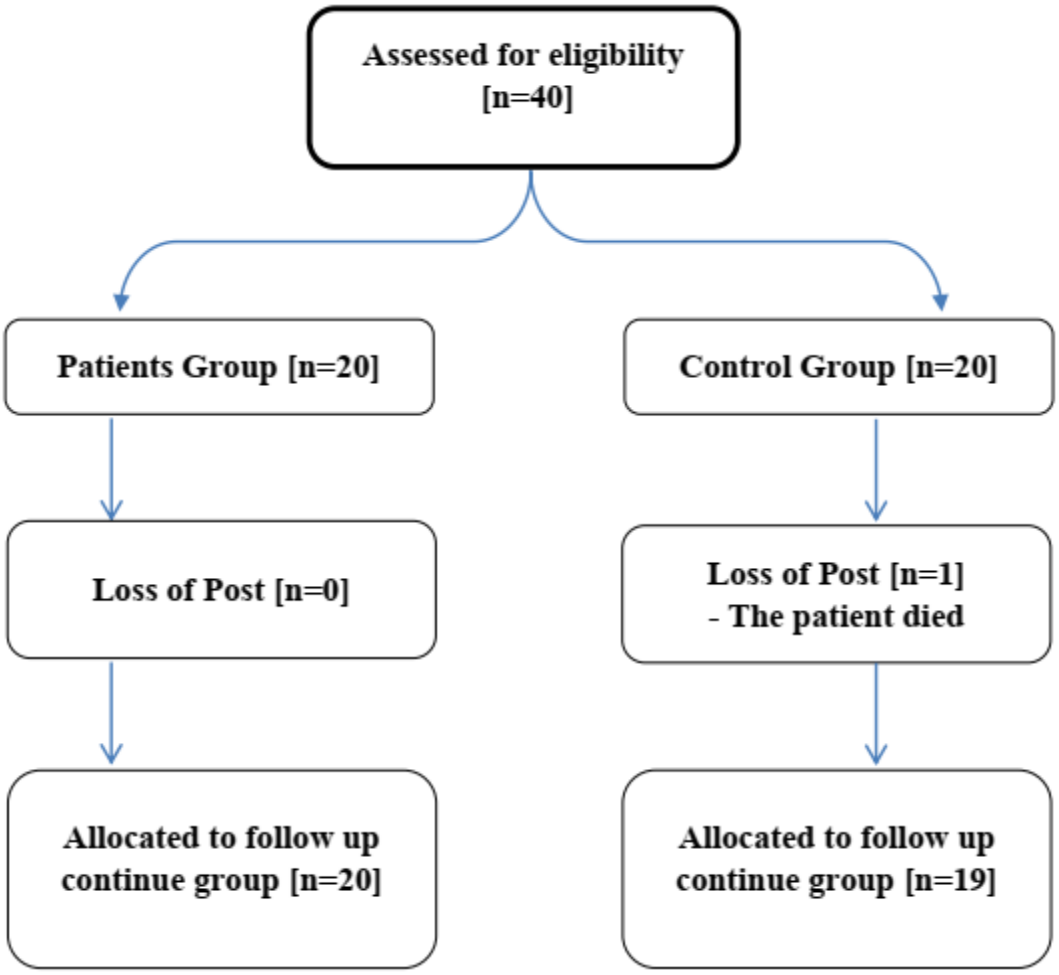

Figure [1]: Flow chart of study participant

Table [1]: General characteristics of the studied groups

Baseline characteristics		Study Group [n=20]	Control Group [n=19]	Test	P-value
Age [years]	Mean ± SD	45.60±11.70	47.75±11.83	-0.578	0.567
	Range	26-59	27-68		
Sex	Female	5 [25.0%]	4 [20.0%]	0.143	0.705
	Male	15 [75.0%]	15 [80.0%]		
Height [cm]	Mean ± SD	163.30±5.90	165.45±6.52	-1.093	0.281
	Range	153-175	153-175		
Weight [kg]	Mean ± SD	79.15±17.81	77.10±18.30	0.359	0.722
	Range	47-115	47-100		
BMI [kg/m^2]	Mean±SD	29.41±6.65	27.70±6.58	0.815	0.420
	Range	18.4-42.76	18.4-42.7		

Table [2]: Pre and post- management mean values of 6MWT, mMRC, FVC in both groups

		Study Group Mean±SD	Control Group Mean±SD	P-value
6MWT [meter]	Pre	236.10±66.04	211.10±60.29	0.219
	Post	332.30±90.03	217.85±60.00	0.001
	p-value	<0.001	<0.001	
mMRC	Pre	3.35±0.49	3.25±0.44	0.503
	Post	2.25±0.55	2.85±0.49	<0.001
	p-value	<0.001	0.002	
FVC [Liter]	Pre	2.16±0.52	2.16±0.49	0.998
	Post	2.22±0.56	2.09±0.61	0.516
	p-value	0.443	0.420	

6MWT: six-minute walk test, **mMRC:** Modified Medical Research Council dyspnea scale, **FVC:** Forced vital capacity.

DISCUSSION

The current study demonstrated that 8 weeks of combined exercise training has caused a significant improvement in, 6MWT and mMRC post management than pre management that were higher in study group compared to control group and non-significantly improve in FVC pre and post in both group and non-significance between both groups.

In a meta-analysis of randomized controlled trials [RCTs], **Reina-Gutiérrez *et al.*** [5] examined the impact of pulmonary rehabilitation on the functional capacity and quality of life in Interstitial Lung Diseases [ILDs], including those caused by coronaviruses. The analysis included 637 ILD patients and revealed a 5.47 percent improvement in forced vital capacity [FVC] and a 44.55-meter increase in the distance covered during the 6-minute walk test [6MWD] compared to their initial measurements. The researchers also provided descriptive information on different types of pulmonary rehabilitation interventions explored in the studies, such as aerobic exercises with resistance training, combined exercises incorporating specific respiratory exercises, and aerobic exercises with specific respiratory muscle training.

With the line of the randomized control study applied by **Okan *et al.*** [11] when preformed 5 weeks of PR [breathing and aerobic exercise] included 52 patients with post covid-19 pneumonia, it was found that the intervention group had a significantly higher value in the posttest 6MWT compared to the control group. Furthermore, within the intervention group, the posttest 6MWT measurement [478.15 ± 67.30 m] was significantly higher than the pretest measurement [423.88 ± 57.19 m]. The intervention group also showed significant differences in FVC values compared to the control group, with a p-value of 0.001. However, there was no significant difference in FVC [L] value when comparing pretest and posttest measurements within the control group. In contrast, the study group exhibited a significant increase in FVC posttest values compared to the pretest measurement [p-value < 0.001]. Also, they stated that there was high significant change in Posttest mMRC values in the control group than the intervention group [p value<0.001] and the intragroup mMRC measurements were significant in both pre and posttest in the intervention group [p value<0.001].

As well, the present study came in line with the **Harputlu *et al.*** [1] who had reached with the evaluation a case report of 68-years-old patient with post COVID -19 fibrosis and found that, in addition to antifibrotic therapy, a personalized outpatient PR program that meets three times a week for eight weeks may improve the patient's respiratory functions, exercise capacity, muscle strength, dyspnea severity, fatigue level, and

involvement in activities of daily living. Incorporating patients with post-COVID fibrosis into comprehensive PR programs and following them for the long term may be necessary, as the study found improvements in exercise capacity and respiratory functions, which may explain why the 6MWT, mMRC dyspnea scale, and dyspnea in activities of daily living were all improved.

The current study also agrees with results reached by **choi *et al.*** [6] who performed 10 sessions of pulmonary rehabilitation, on case report with A 59-year-old man with pulmonary fibrosis after COVID-19 suggested that exercise-based PR helped patients with this condition. and showed improvements were seen in 6MWT and mMRC according to the functional assessment.

The current study in the line with **Ali *et al.*** [12] who confirmed after pulmonary rehabilitation on single case of 72 years old man with post COVID-19 pulmonary fibrosis could perform Activity of Daily Living [ADL] without minimal support or supervision, also reported significant improvement in functional evaluation of 6MWT and mMRC. In concurrent with the present study **Elganady *et al.*** [15] stated that There was statistically significant improvement regarding 6MWT [p value ≤0.001], mMRC scale [p = 0.001] after 6 week of pulmonary rehabilitation program on 20 ILD patients and also non-significant improvement FVC.

Nishiyama *et al.* [16] performed pulmonary rehabilitation on 30 patients with ILD and confirmed that after 10 weeks of rehabilitation there were significant improvements in the 6MWD with p value [p <0.05] and no significant improvement in pulmonary function variables [FVC] so this is concurrent with current study.

In concurrent with current study, **Choi *et al.*** [17] did not confirm any improvement in PFT[FVC] variables values between the groups after eight weeks of PR on 25 patients with IPF, also reported the significant improvement in 6MWT values after PR in the PR group with p value = 0.002.

Also, **Sciriha *et al.*** [18] reported; after 12 weeks of Pulmonary Rehabilitation program for 60 patients with ILDs resulted in significant improvement in 6MWT [P value = 0.001] and no significant changes were found in FVC [p = 0.832].

In contrary to the results of the current study, **Jackson RM *et al.*** [19] reported no significant improvement in 6MWT in rehabilitation and control group = 0.818, 0.289 respectively, after 12 weeks of the exercise training program for 22 Idiopathic pulmonary fibrosis [IPF] patients in his randomize control trail.

In contrary to the results of the present study **Perez-Bogerd *et al.*** [20] reported that there was no discernible change in mMRC and physical activity after the rehabilitation program [8-12 weeks] for 60 patients with ILDs. Nevertheless, the present study was in agreement with previous research showing that PR had no effect on pulmonary function test [PFT], with the exception of forced vital capacity, which showed a slight improvement in the rehabilitation group when compared to usual care, however there was significant improvement in 6MWT with p value < 0.001 which concurred with current study.

The patients' positive response to combined exercise training led to significant improvement in their condition. The patients' willingness to participate in the exercise and follow the rehabilitation protocol played a major role in their progress. Throughout the study, informal feedback was noted, indicating that patients exhibited tolerance and acceptance of the combined exercise approach. This feedback suggests that the approach could be considered a safe and effective rehabilitation protocol. It has the potential to partially reverse the adverse effects of pharmacological treatment in post COVID-19 pulmonary fibrosis patients, leading to symptom relief and improved daily activities.

Conclusion: It was concluded that patients with post COVID-19 pulmonary fibrosis decreased functional capacity with a diminished physical, functional, emotional and psychological status. combined exercise training [consisting of aerobic, resisted training] and breathing exercises is recommended in Post COVID-19 pulmonary fibrosis conditions along with the pharmalogical treatment following the guidelines of pulmonary fibrosis. So combined exercise training [consisting of aerobic, resisted and breathing exercises] contribution decreasing patients' physical and functional disabilities, promoting a much more independent and functional lifestyle.

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