



Early View

Correspondence

Pulmonary rehabilitation in Covid pneumonia sequelae: so near yet so far

Aqeel Hussain, Alkesh Kumar Khurana, Abhishek Goyal, Raj Krishnan Soman

Please cite this article as: Hussain A, Khurana AK, Goyal A, *et al.* Pulmonary rehabilitation in Covid pneumonia sequelae: so near yet so far. *ERJ Open Res* 2021; in press (<https://doi.org/10.1183/23120541.00398-2021>).

This manuscript has recently been accepted for publication in the *ERJ Open Research*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

Copyright ©The authors 2021. This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact permissions@ersnet.org

Pulmonary Rehabilitation in Covid pneumonia sequelae: So near yet so far.

Authors & Affiliations:

1. Aqeel Hussain
Senior Resident
Pulmonary Medicine
AIIMS Bhopal
aqeelturabi09@gmail.com
2. Alkesh Kumar Khurana (Corresponding Author)
Associate Professor
Pulmonary Medicine
AIIMS Bhopal
alkesh.pulmed@aiimsbhopal.edu.in
3. Abhishek Goyal
Additional Professor
Pulmonary Medicine
AIIMS Bhopal
abhishek.pulmed@aiimsbhopal.edu.in
4. Raj Krishnan Soman
Senior Resident
Pulmonary Medicine
AIIMS Bhopal
rksut1688@gmail.com

Pulmonary Rehabilitation in Covid pneumonia sequelae: So near yet so far

We read with great interest the article by Gloeckl et al whereby they have done an interesting study to evaluate the effect and feasibility of Pulmonary Rehabilitation (PR) in Covid patients.[1] However, we feel that a few pertinent issues need to be highlighted and addressed. Covid-19 associated chronic health issues can persist for prolonged period after recovery from acute illness and has been termed as long covid. However the literature suggests that CT changes and associated lung function impairment show resolution with time.[2]

Firstly, to determine the effect of any intervention in presence of spontaneous recovery, a control group representative of the patient population is needed. Post covid patients who could not be offered PR because of barriers like patient refusal, language difficulties could have been enrolled as controls and followed over time to compare their improvement with the PR group. The relevance of having a control group in this study is even more as the improvement in Six minute walk distance (6MWD) in this study can be attributed to multiple confounding factors like spontaneous improvement in lung function, increased motivation at the time of completion of PR and learning effect rather than claiming it solely to be the effect of PR. In mild-moderate group, a 7.7% increase in FVC was seen and in severe-critical group 11.3% increase in FVC was seen. As a positive correlation between FVC and 6MWD is well documented in literature [3,4,5], the increase in 6MWD can be contributed at least in part to the spontaneous improvement in the lung function. This is even more relevant in the mild-moderate subgroup where the improvement in 6MWD was relatively lesser (48m). Also a practice 6MWT was not performed, improvement in the 6MWD on follow up might have got confounded by learning effect. Thus the spontaneous recovery seen in the covid related lung function impairment and the presence of other confounding factors potentially contributing to the increase in 6MWD makes a covid control group for comparison even more necessary before labelling the change as an effect of PR especially in mild-moderate group. Also, the inclusion of patients with idiopathic pulmonary fibrosis as control (non-PR IPF control) in this scenario is not feasible as the two diseases don't share pathophysiology and hence differ in their natural course. While lung functions usually improve in patients of covid-19 with time, in IPF lung functions progressively decline with the progression in fibrosis. This disparity in the lung function change was noticed in this study also as in the cohort of non-PR IPF patients of this study, the DLCO decreased by 1% whereas it increased in patients with mild-moderate Covid-19 by 4.5% and in severe/critical COVID-19

patients by 3.7%. Similarly the FVC of non-PR IPF group increased by 1% as compared to patients with mild-moderate and severe/critical COVID-19 where it increased by 7.7% and 11.3% respectively. So using a group of patients with significantly different natural course as compared to covid-19 does not look feasible.

Secondly, the improvement in both the mental quality of life and depression can also contribute to the improvement in 6MWD by contributing to a positive outlook in the patients at the time of completion of the PR. High motivation has been mentioned as a source of variability for the 6MWD [7] and thus the improvement in mental quality of life might also have contributed to improvement in 6MWD, at least in part. This component could also have been addressed in presence of a matched control group.

Thirdly, the subset of patients in mild/moderate group did not even require oxygen supplementation and considering them for rehabilitation on the basis of symptoms of dyspnoea, fatigue, cough, cognitive impairment only without significant functional limitation needs a second thought. As per previous studies, the median 6MWD for healthy men is approximately 580 m and for healthy women is 500m. [7] The 83% of patients in the mild-moderate group in this study were females(20 out of total 24) and the mean 6MWD of this group mentioned is 509m. The baseline values of 6MWD in the mild/moderate group were almost in the normal range and so in this group the difference observed in the 6MWD can be attributed to usual variability seen in 6MWD rather than effect of PR. A baseline almost normal 6MWD is obviously expected to result in suboptimal increase after PR intervention. As Ryerson et al had shown that in ILD a baseline significantly decreased 6MWD is a predictor of improvement in 6MWD with PR ($r=-0.49$, $p<0.0005$).[8] Therefore expecting a normal 6MWD to increase after an intervention when it is normal/near normal at baseline does not look feasible. The lack of any significant effect of PR on the prevalence of covid symptoms (dyspnoea, fatigue, cough, cognitive impairment) assessed by interviewing the patients after PR further challenges the rationale of considering this particular cohort for benefits of PR.

Lastly, PR services offered to patients differed from the standard practice followed in other respiratory diseases in both the mode and duration of PR program. PR services are usually offered for at least 6 weeks as an out-patient program rather than only for 3 weeks as an in-patient program as offered in this study. Previously PR of 4 weeks has been studied and

found to be less effective than 7 week PR even in COPD where the benefits of PR are larger in magnitude as compared to any other chronic respiratory diseases.[9] So a duration of 3 weeks only seems too little to determine the effects of any intervention on parameters assessed.

We do appreciate the authors for exploring this new dimension of management of Covid patients but the above mentioned points need to be addressed before the results are imbibed in their true sense. The realistic application of an old tool of PR in a new disease of Covid pneumonia needs further research in a more planned and comprehensively designed study.

References:

1. Gloeckl R, Leitl D, Jarosch I, Schneeberger T, Nell C, Stenzel N, et al. Benefits of pulmonary rehabilitation in COVID-19: a prospective observational cohort study. *ERJ Open Res.* 2021 May 31;7(2):00108-2021. doi: 10.1183/23120541.00108-2021.
2. González J, Benítez ID, Carmona P, Santistevé S, Monge A, Moncusí-Moix A et al. Pulmonary Function and Radiologic Features in Survivors of Critical COVID-19: A 3-Month Prospective Cohort. *Chest.* 2021 4:S0012-3692(21)00464-5. doi: 10.1016/j.chest.2021.02.062.
3. Agrawal MB, Awad NT. Correlation between Six Minute Walk Test and Spirometry in Chronic Pulmonary Disease. *J Clin Diagn Res.* 2015;9(8):OC01-4. doi: 10.7860/JCDR/2015/13181.6311.
4. Ameri H. Six minute walk test in respiratory diseases: A university hospital experience. *Ann Thorac Med.* 2006;1(1):16.
5. Asmita M, Kumari Indira KS. Correlation of Six Minute Walk Test with Spirometry and DLCO in Chronic Respiratory Diseases: a tertiary care hospital experience. *Pulmon.* 2011;13(2):55–9.
6. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002 1;166(1):111-7.
7. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998;158:1384–1387.
8. Ryerson CJ, Cayou C, Topp F, Hilling L, Camp PG, Wilcox PG, et al. Pulmonary rehabilitation improves long-term outcomes in interstitial lung disease: a prospective cohort study. *Respir Med.* 2014 ;108(1):203-10. doi: 10.1016/j.rmed.2013.11.016.

9. Green RH, Singh SJ, Williams J, et al. A randomised controlled trial of four weeks versus seven weeks of pulmonary rehabilitation in chronic obstructive pulmonary disease. *Thorax* 2001;56:143–5.