Pulmonary rehabilitation in COVID-19 pneumonia sequelae: so near yet so far

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To the Editor:

We read with great interest the *ERJ Open Research* article by Gloeckl *et al.* [1] where the authors performed an interesting study to evaluate the effect and feasibility of pulmonary rehabilitation (PR) in coronavirus disease 2019 (COVID-19) patients. However, we feel that a few pertinent issues need to be highlighted and addressed. COVID-19-associated chronic health issues can persist for a prolonged period after recovery from acute illness and have been termed "long COVID". However, the literature suggests that computed tomography changes and associated lung function impairment show resolution with time [2].

First, to determine the effect of any intervention in the presence of spontaneous recovery, a control group representative of the patient population is needed. Post-COVID-19 patients who could not be offered PR because of barriers like patient refusal or 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 greater, as the improvement in 6-min 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 the mild/moderate group, a 7.7% increase in forced vital capacity (FVC) was seen and, in the severe/critical group, a 11.3% increase in FVC was seen. As a positive correlation between FVC and 6MWD is well documented in the literature [3–5], 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 less (48 m). Also, a practice 6-min walk test was not performed, so improvement in the 6MWD on follow-up might have been confounded by learning effect. Thus, the spontaneous recovery seen in the COVID-19-related lung function impairment and the presence of other confounding factors potentially contributing to the increase in 6MWD makes a COVID-19 control group for comparison even more necessary before labelling the change as an effect of PR, especially in the mild/moderate group. Also, the inclusion of patients with idiopathic pulmonary fibrosis (IPF) as a control (non-PR IPF control) in this scenario is not feasible, as the two diseases do not share pathophysiology and hence differ in their natural course. While lung function usually improves in patients of COVID-19 with time, in IPF lung function progressively declines 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 diffusing capacity of the lung for carbon monoxide 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 the 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. Thus, using a group of patients with a 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 could 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 [6] 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 the presence of a matched control group.

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To evaluate the benefit of pulmonary rehabilitation, a control group is a must to mitigate the effect of confounding factors like spontaneous resolution of lung damage, learning effect and better mental status https://bit.ly/3qy5sfe

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Thirdly, the subset of patients in the mild/moderate group did not even require oxygen supplementation and considering them for rehabilitation on the basis of symptoms of dyspnoea, fatigue, cough and 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 500 m [7]. 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 was 509 m. 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 to an effect of PR. A baseline almost normal 6MWD is obviously expected to result in suboptimal increase after PR intervention. As Ryerson *et al.* [8] have shown, in interstitial lung disease a baseline significantly decreased 6MWD is a predictor of improvement in 6MWD with PR ($r=-0.49$, $p<0.0005$). 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-19 symptoms (dyspnoea, fatigue, cough, cognitive impairment) assessed by interviewing the patients after PR further challenges the rationale of considering this particular cohort for the 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 programme. PR services are usually offered for at least 6 weeks as an outpatient programme rather than only for 3 weeks as an inpatient programme as offered in this study. Previously, PR of 4 weeks has been studied and found to be less effective than 7 weeks of PR, even in COPD where the benefits of PR are larger in magnitude as compared to any other chronic respiratory diseases [9]. Thus, a duration of only 3 weeks 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-19 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 to a new disease of COVID-19 pneumonia needs further research in a more planned and comprehensively designed study.

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