Review 1: "Persistent Inflammatory Interstitial Lung Disease Following SARS-CoV-2 Infection at 6 Weeks Post Discharge Responds Rapidly to Oral Corticosteroids"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

Myall et.al report an observational study of persistent inflammatory interstitial lung disease of patients from a single center at 6 weeks post SARS-CoV2 infection who responded to short courses of oral prednisolone. These patients were identified amongst 1333 patients who were admitted with SARS-CoV2 pneumonitis between February and May 2020. Whilst 30 patients have been commenced on prednisolone, the authors report the treatment response in 13 patients and felt compelled to report their interim findings in order to alert the wider community of this sequelae of SARS-CoV2. The authors are to be congratulated in being able to coordinate this follow-up amidst an ongoing pandemic. I have the following comments:

- 1) Please clarify the original cohort? Was it 1333 (as in flow chart) or 1272 as stated in body of manuscript? The majority were PCR positive but did all have pneumonitis?
- 2) Of your initial cohort, 139 were too unwell to attend. Was it related to their respiratory status? Surely, this is the cohort that needs to be followed up with.
- 3) Who conducted the telephone calls at 4 weeks? Was the telephone call structured? Were specific questionnaires used?
- 4) Of the 138 patients who had symptoms but no physiologic impairment or abnormal CXR—how sure are you that they didn't have ongoing mild pneumonitis given the wide range of normal PFT values and that CXR is not sensitive of mild changes?
- 5) In those with functional or physiological impairment (n=103) in the absence of radiological evidence of persistent disease or PE—they were referred on to other

services. Did they have CT chest before moving on? I am not clear exactly when CTs were done in your structured assessment.

6) Under "Patient characteristics"—please clarify at the start how many patients were described in this cohort. I assume that there were 35 patients.

7) I have never seen 6MWT distance described as % predicted. I don't think this is helpful.

8) Please standardize expression of mean FVC and mean DLco—were they really normally distributed—if not please express as median and range. Looking at your FVC and DLco, there are patients who had normal PFT. I assume that they were deemed abnormal based on their CXR findings.

9) Table 1—please change number of males to 25.

10) What was the standard of care at the time? 6 received steroids whilst 19 received ICU care—what was the basis of receiving steroids? The use of dexamethasone is now standard of care in patients who need supplemental oxygen. I realize the recovery trial was published in July 2020 after your cohort of patients were recruited. But was there any correlation in steroid use and the development of OP? I think this is worth discussing. I think it might be also worth speculating as to whether OP would be less common with a latter cohort of survivors where dexamethasone is part of standard care in patients who need supplemental oxygen acutely.

11) Were there any risk factors that predicted the development of OP/pneumonitis. How many patients were ventilated? Do you think some of these changes could relate to ventilator-associated complications? I realize that the numbers are too small to make any conclusions but nevertheless they serve as interesting observations.

12) Table 5—n=10 but 13 patients completed treatment.

13) KCO does not add value—I suggest that you drop this to simplify things.

14) Fig. 2 is essentially table 5—this is redundant.

15) Page 4 line 2—did you mean gas transfer or arterial blood gas?

16) What was the outcome of patients with GG and <15% involvement not offered treatment and repeat CT further 3 months? Why was a cut-off of 15% used to dichotomize treatment?