Reviewer’s report

Title: Comparison of disease progression subgroups in idiopathic pulmonary fibrosis

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Reviewer: Felix Chua

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Comparison of disease progression subgroups in idiopathic pulmonary fibrosis

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I enjoyed reading this manuscript which conveys a useful clinical message. However, several key points require clarification.

1. The authors used the 2011 ATS/ERS/JRS/ALAT guideline to categorise the HRCT pattern of disease. Confusingly, they have used the diagnostic radiological term 'probable UIP' which was only proposed in the 2017 Fleishner white paper and the latest 2018 ATS/ERS/JRS/ALAT guideline. Can the authors please clarify? 'Probable UIP' was indeed applied in 2011 but only as a histopathological description, not on CT.

2. Out of 131 patients with HRCT for evaluation, 81 were felt to satisfy criteria for 'definite UIP' - this seems high in light of other grouped analyses reporting a rate between 30 - 40% (e.g. 35% in the INPULSIS study). Can the authors please comment on this sizeable disparity?

3. Assuming that the rate of 'definite UIP' is truly 61% as they authors contend, then it would be helpful to have a comment on the lack of influence of honeycombing on the rate of disease progression since roughly a third of cases met criteria for each of the three subgroups, i.e. rapid, moderate and slow progression respectively, despite the presence of definite UIP in nearly two-thirds of the whole cohort. As an extension, it would also be informative to know how many cases of definite UIP were present in each of these three subgroups. This is a point of particular interest since other reports have suggested that honeycombed and non-honeycombed UIP progress at a comparable rate.

4. Of the 21 cases with a non-UIP pattern on CT, 12 underwent surgical biopsy and in all 12 cases, histological UIP was revealed. Can the authors please clarify if these 12 cases met the ancillary CT criteria to achieve an overall diagnosis of UIP, i.e. did their CT also show subpleurally based fibrosis with traction bronchiectasis in multiple lobes, and thus qualify for inclusion in the current study? Or did their CTs show changes of an alternative diagnosis (e.g. fibrotic HP) where a biopsy finding of UIP may also have been conceivable? If their CTs showed a truly non-UIP pattern (even though the histology was consistent with UIP), a discussion of discordance would be helpful.
5. From the previous point, I assume there were 9 cases who had a CT pattern of non-UIP and who did not undergo lung biopsy. If so, how did the authors justify including these 9 cases in a study of UIP?

6. Regarding the three subgroups with a different rate of disease progression - data in table 2 - it may be helpful to briefly discuss the possibility that a higher mean DLco is the reason why there are more GAP I patients in the slow group and more GAP II patients in the moderate group. It cannot after all be an FVC effect since this parameter is no different between the moderate and slow progressors.

7. Whilst DLco is acknowledged and shown to be an important determinant of both the rate of disease progression and survival, there is no discussion of pulmonary hypertension as a possible contributor to impaired gas transfer. Can the authors offer any information on the presence of PH in the three subgroups?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

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