Peer Review File
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Reviewer A

In the present study, the authors investigate various diagnostic criteria for the diagnosis of progressive pulmonary fibrosis. The three criteria primarily differ in terms of progression at 6, 12, and 24 months. The authors conclude that both the 12-month and 24-month criteria are adequate for defining progressive pulmonary fibrosis for both clinical and scientific purposes, with DLCO serving as an independent factor.

From my perspective, the results are not surprising, as the included criteria such as FVC, decrease in DLCO, and the coarse analysis of HR-CT are expected to show an effect only later due to the variability of results within the patient group and their low sensitivity. Since FVC hardly differs between the three categories, it is not surprising that the desired results only allow discrimination after 12 or 24 months. This, in my view, is inherent in the nature of the chosen parameters and their threshold. But also due to the chosen population.

Comment 1：

The following additional points are unclear from my perspective. It remains unclear whether patients with IPF were included or incorporated.
Reply 1: Thanks for the reviewer's comment. The patients with IPF were excluded in the cohort, which has been added in methods (line 28-30, and line 36-37, page 3).
Changes in the text: The following sentences were added, 'Patients with diagnosis of IPF or with antifibrotic therapy more than 6 months were excluded from the cohort', and 'Patients with IPF and probable IPF were excluded for the assessment of progressive fibrosing'.

Comment 2:
The authors mix the terms of pattern-based UIP with the clinical definition of IPF. This needs to be better elaborated in the patient description. In the results section, this became more apparent.
Reply 2: Thanks for the suggestion. We had elaborated the definition of UIP and IPF in methods. (Line 34-35, page 3.)
Changes in the text: The UIP pattern defines the typical changes of IPF in radiology and pathology. However, it's not a clinical diagnosis.

Comment 3:
The results are partially unclear and difficult to read. In my view, information is missing regarding the extent to which the initial definition of the disease has influenced the courses. This also seems to be reflected in the comparison of various studies in the discussion.

Reply 3: Thanks for the reviewer's reminding. Honestly, the disease courses were influenced by the definition of the PPF, which was studied by this paper. And the studies in comparison used the same definition of PPF (two-year standard)[1-3].

Comment 4:
From my standpoint as a radiologist, this study also shows that the criteria applied by pneumologists can only detect progressive pulmonary fibrosis late due to their low sensitivity, and that imaging parameters might be able to recognize certain tendencies earlier in the context of radiomics, as some studies have already shown.
Reply: We totally agree with the reviewer's viewpoint. The related discussion had been added in the revised manuscript. Thanks.
Changes in the text: With the application of artificial intelligence in radiology, some studies have already shown that imaging parameters might be able to recognize progressive tendencies earlier than the traditional parameters. (line 1-3, page 8)

Reviewer B

Authors investigated the difference of three diagnostic criteria of PPF, and concluded that the one-year and two-year criterion are the reasonable choice to define PPF. This study seems to be useful for the clinical practice, but I have some concerns in this study. My comments are as follows.

1. In Abstract, DLCO was not spelled out.

Reply: Thanks for pointing out the omission, and we had corrected it.
Changes in the text: In multivariate Cox model, only baseline predicted percent diffusing capacity of the lungs for carbon monoxide (DL_{CO}%) <50% was correlated with mortality, with a hazard ratio of 3.4 (95% CI 1.1-10.6, P=0.03).

2. In Methods, authors said that "with antifibrotic therapy more than 6 months were excluded." Does it mean that the patients with ongoing antifibrotic therapy within 6 months were included? I think the patients with ongoing antifibrotic therapy should be excluded irrespective of the duration.

Reply: Thanks for the suggestion so much. First, we admit that the antifibrotic therapy have influence on results of the study. We reviewed the raw data of our cohort and found that 11 patients (Nintedanib 9; Pirfenidone 2) received the antifibrotic therapy. Among them, 6 patients were included in the PPF group (all 3 criteria). The average time of the antifibrotic treatment was 2.6 (±1.0m) months. Besides, these patients initiated the antifibrotic therapy after they were evaluated by the criteria of PPF, and they had no data of pulmonary function after they began the antifibrotic therapy. As a result, the antifibrotic therapy had very small impact on our results.
Changes in the text: The related explanation was added in the limitation of the study (line 1-8, page 9). 'Third, we included the patients with antifibrotic therapy within 6 months, which might impact on analysis of survival and pulmonary function. However, we reviewed the raw data of our cohort and found that only 11 patients (Nintedanib 9;

Pirfenidone 2) received the antifibrotic therapy. Among them, 6 patients were included in the PPF group (all 3 criteria). The average time of the antifibrotic treatment was 2.6 (±1.0m) months. Besides, these patients initiated the antifibrotic therapy after they were evaluated by the criteria of PPF, and they had no recheck data of pulmonary function during the time of antifibrotic therapy. As a result, the antifibrotic therapy had very small impact on our results.'

3. From Tables E2-4, the total sample size would be 3331. But the main text and Table E1 said it was 2476, which were conflicting.

Reply: Thanks very much for reminding the mistake. Because of our carelessness, patients with IPF were taken into statistical analysis in Table E2-4. And we had corrected Table E2-4 in the revised version.

Changes in the text: The Table E2-4 had been corrected.

4. In Tables 2 and E2-4, P value should be shown.

Reply: Thanks for the suggestion. We had added P value in the corresponding tables.

Changes in the text: P value had been added in Table 2 and E2-4.

Reviewer C

GENERAL COMMENTS:

The authors retrospectively examined adult patients with fibrotic ILD for three predefined diagnostic criteria of PPF, assessing the disease progression in the preceding 6, 12, and 24 months. They found that the average one-year decline in FVC% was -1.0%, -2.7%, and -4.1% for three groups, and the 4-year survival rate was 74%, 66%, and 62%. A multivariate Cox model demonstrated that only baseline DLco%<50% was correlated with mortality. The authors conclude that the one-year and two-year criteria are reasonable choices to define PPF in research and clinical practice, and DLco% is an independent predictor for mortality of PPF. This report includes valuable information but has several concerns.

MAJOR COMMENTS:

1. Rationale of the study

The authors state that till now, researchers have proposed three diagnostic criteria for PPF, which assess the progression in the preceding 6, 12, and 24 months. However, in the reference for evaluating progression in the prior six months, eligible patients had progressive fibrosing unclassifiable ILD with %FVC of 45% or higher and %DLco of 30% or higher, more than 10% fibrosis on HRCT, and an HRCT from the previous 12 months, not six months (Lancet Respir Med, 2020). Therefore, the study's goal to compare the three different diagnostic criteria is irrational.

Reply: Thanks for the reviewer's comment. We reviewed the reference again, and found that the above-mentioned 'previous 12 months' were describing that, patients should take the HRCT examination in previous 12 months, not for evaluation of progression. And the progression was defined as follow: progressive disease, defined

as either a more than 5% absolute decline in percent predicted FVC or significant symptomatic worsening not due to cardiac, pulmonary (except worsening of underlying unclassifiable ILD), vascular, or other causes (as determined by the investigator) **within the previous 6 months**[4].
Changes in the text: None

2. Diagnostic criteria of PPF
The authors defined PPF by three criteria: 1) In the preceding six months, an absolute decline in FVC% over 5% or significant symptomatic worsening; 2) at least two of the three criteria in the preceding 12 months: worsening respiratory symptoms; an absolute decline in %FVC >5% or an absolute decline in %DLco% >10%; radiological evidence of disease progression; 3) In the preceding 24 months, an absolute decline in %FVC >10%, or an absolute decline in predicted %FVC of 5–10% with worsening respiratory symptoms or increased fibrosis on HRCT, or worsening respiratory symptoms and increased fibrosis on HRCT. The authors should clearly state differences between (1) significant symptomatic worsening and (2 and 3) worsening respiratory symptoms and between (2) radiological evidence of disease progression and (3) increased fibrosis on HRCT.
Reply: Thanks for the reviewer's suggestion. We totally agree that it is important to clearly describe the difference of the definition. There is no actual difference between the symptomatic worsening and worsening respiratory symptoms, and between radiological evidence of disease progression and increased fibrosis on HRCT. We used different description for the reason that we take the text originally from the reference. Besides, for the readability of article, we avoid using the same text. But after the reviewer's reminding, we agreed to use the same description here, in order to convey a more precise definition.
Changes in the text: We uniformly used 'worsening respiratory symptoms' and 'increased fibrosis on HRCT' in all three criteria. (Line 41-42, page 3; Line 3-4, page 4)

3. Overlap of study subjects
The authors identified 246 PPF patients by the half-year standard, 154 patients, 139 by the one-year standard, and 281 patients by the two-year standard. Among them, 95% or 147 patients in the one-year group also belonged to the two-year group. Therefore, it is plausible that their conclusion was the one-year and two-year criteria are reasonable choices to define PPF in research and clinical practice. If the authors aim to compare their criteria, they should pick up 121 patients who solely belong to the half-year group, five one-year group cases, as well as 92 two-year patients.
Reply: We appreciated for the reviewer's comment. In current study, we found that 95% or 147 patients in the one-year group also belonged to the two-year group. So, for further comparison, we selected out the patients meeting to half-year criteria but not the one-year criteria (n=154), and meeting to two-year criteria but not the one-year criteria (n=134), then we compared these patients with group of One-year (Figure 3). And we found that group of two-year and group of one-year had similar decline trend of FVC%,

and similar survival rate after 4-year follow up. However, there were significant differences in FVC% decline and survival rate between group of half-year and group of one-year. Based on these results, we concluded that clinical practitioners should make flexible application with the one-year and two-year criteria, especially for those meeting the two-year standard, but not the one-year standard, which take a certain portion of ILD patients in the real-world situation of China.

Changes in the text: For further comparison, we selected out the patients meeting to half-year criteria but not the one-year criteria (n=154), and compared these patients with group of One-year (Figure 3). Patients in half-year group had higher survival rate (P=0.004), and milder decrease of FVC% (P<0.001) compared with one-year group. Then the similar analyses were conducted between two-year and one-year group. Patients in group of two-year had higher survival rate (P=0.02), and milder decrease of FVC% (P=0.002) compared with one-year group. However, at time of the 4th year, there was similar survival rate and FVC% changes in group of two-year and one-year. Besides, compared with group of one-year, group of two-year had 1.59% less decline of FVC%. But, the decline of FVC% was 6.53% less in group of half-year, compared with one-year group. (line 4-14, page 6)

MINOR COMMENTS:

1, DLCO should be DLco.

Reply: The DLCO has been changed into DLco in the text**.** Thanks very much.

Reviewer D

The present study suggested that 1-year and 2-year PPF criteria are more reasonable than half year criteria and baseline DLCO is independent prognostic factor in ILD. This paper has large population, but has some problem as follows.

Major comments

1. I consider that the reason why the 1-year and 2-year PPF criteria are reasonable is not sufficiently explained, so please add an explanation. It is not sufficient if this reason is that cases meeting to the 1- and 2-year PPF criteria overlap well and have a worse prognosis than the half-year criteria.

Reply: Thanks for the reviewer's suggestion. For further comparison, we selected out the patients meeting to half-year criteria but not the one-year criteria (n=154), and meeting to two-year criteria but not the one-year criteria (n=134), then we compared these patients with group of One-year (Figure 3). And we found that group of two-year and group of one-year had similar decline trend of FVC%, and similar survival rate after 4-year follow up. However, there were significant differences in FVC% decline and survival rate between group of half-year and group of one-year. Based on these results, we concluded that clinical practitioners should make flexible application with the one-year and two-year criteria, especially for those meeting the two-year standard, but not the one-year standard, which take a certain portion of ILD patients in the real-world situation of China.

Changes in the text: For further comparison, we selected out the patients meeting to half-year criteria but not the one-year criteria (n=154), and compared these patients with group of One-year (Figure 3). Patients in half-year group had higher survival rate (P=0.004), and milder decrease of FVC% (P<0.001) compared with one-year group. Then the similar analyses were conducted between two-year and one-year group. Patients in group of two-year had higher survival rate (P=0.02), and milder decrease of FVC% (P=0.002) compared with one-year group. However, at time of the 4th year, there was similar survival rate and FVC% changes in group of two-year and one-year. Besides, compared with group of one-year, group of two-year had 1.59% less decline of FVC%. But, the decline of FVC% was 6.53% less in group of half-year, compared with one-year group. (line 4-14, page 6)

2. Method: Please explain why the diagnostic criteria for PPF was based on the 2022 global guidelines (reference 13), but the that for IPF based on the 2018 guidelines (reference 14) but not the 2022 version.

Reply: We are sorry for the careless omission. We actually used the latest version of IPF guideline, and we had revised the reference information. Thanks for the remind.
Changes in the text: In the method part, we had updated the reference information in the revised manuscript.

3. Line 102: As the criteria for UIP patterns on the HRCT are not sufficiently presented, please show which criteria were followed. Please show the full name of UIP, which is the first word, not an abbreviation.

Reply: Thanks for the reviewer's suggestion. We also followed the criteria from the latest IPF guideline, and we added the definition of UIP in method (line19-20, page 4).
Changes in the text: UIP pattern on HRCT was defined as basal and subpleural predominant honeycombing opacities associated with traction bronchiectasis5. HRCT was evaluated by two experienced radiologists separately.

4. Line 157: I am sorry. I am unable to decipher the meaning of the following research results, could you please elaborate? How is this result read from figure 2?

"Only the time interval for PFT measurement was correlated with FVC% change (Figure 2, *P*<0.001)."
Reply: We are sorry for not describing the results clearly. In this part, we used mixed effect model to evaluate the factors affecting FVC% decline, which included time interval for the PFT measurement, age, sex, smoking history, baseline FVC% and DLco%. In other words, these factors were treated as the independent variables, and the change of FVC% was treated as dependent variable.
Changes in the text: We used mixed effect model to evaluate the factors affecting lung function decline. In the model, we evaluated influences of fixed effects on changes of FVC%, which included time interval for the PFT measurement, age, sex, smoking history, baseline FVC% and DLco%. Only time interval for PFT measurement was correlated with FVC% change (Figure 2, P<0.001). (line34-37, Page 5)

5. Table 2: Results (lines 147 to 155) show some two-group comparison of clinical data among the half-year, 1-year, and 2-year groups with significant difference. P-values for all comparisons of clinical data should be presented in table 2. Two-group comparisons should be Bonferroni-corrected.

Reply: Thanks for reviewer's suggestion. We had added P value in the table 2.

Changes in the text: P value had been added in Table 2 and E2-4.

6. Table 3: What is the rationale for setting the cutoff values for baseline FVC (60%), DLco (50%) and Age (60%)?

Reply: We are sorry for not explaining this issue in the manuscript. The cutoff values were selected out according to the references[1,6] and the data characteristics of the cohort. On the one hand baseline FVC% and DLco% were used as the risk factors in the Cox analyses. On the other hand, we tried to use the media values, so that we got the similar sample size in each group. Besides, Nasser and his colleges had explored influence of age on survival of PPF, and they found the patients between 60-75 had significant worse prognosis than younger patients. So we used 65 as the cutoff value.

Changes in the text: The cutoff value were selected out according to the references and the median value of the cohort**.** (line 3-4, page 5)

Minor comments

Please subscript the LCO of the DLCO.

Reply: Thanks for the suggestion. We had subscripted the LCO of the DLCO.