Author's response to reviews

Title: Clearance of Technetium-99m-DTPA and HRCT Findings in the Evaluation of Patients with Idiopathic Pulmonary Fibrosis

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Author's response to reviews: see over
POINT-BY-POINT REPLY

Reviewer: 1

We would like to thank you very much for your helpful comments and suggestions. We have revised our manuscript accordingly. A point-by point answer follows.

COMMENT: Performing the HRCT score of extent, the Authors did not try to separately evaluate the fibrotic component (reticular opacities, honeycombing, ground glass with bronchial or bronchiolar dilatation) from possible activity signs (areas of ground glass or consolidation without reticular opacities or bronchial dilatation). It could be of some interest to add this kind of evaluation, in comparison with scintigraphic and BALF findings.

REPLY: Thank you for this question. In our first evaluation HRCT scoring included extent of: a. ground glass opacities without evidence of bronchiolectasis and bronchiectasis (GG); b. fine reticulation including areas of ground glass opacities with coexisting bronchiolectasis and bronchiectasis, (FR); and c. coarse reticulation-honeycombing (CR). Composite scores of disease extent included the fibrosis score, composed by the extent of both fine and coarse reticulation and the total interstitial disease score (TIDs) composed by the sum of all the above-mentioned scores. On the other hand, as we did not detect a correlation between the extent of GG, FR or CR and DTPA clearance, lung function or BALF cellularity, we favoured to exclude these sub-categories from our manuscript.

Again, thank you very much for your constructive comments

On behalf of the authors,

Professor Demosthenes Bouros
Reviewer: 2

We would like to thank you very much for your helpful comments and suggestions. We have revised our manuscript accordingly. A point-by-point answer follows.

Comments to the Author

General: Interesting but reads negatively when the data suggests a positive correlation. There is a correlation which is weak but in a small group of patients is noteworthy.

REPLY: Thank you for this question. We found a moderately significant correlation of DTPA clearance with the visual score in HRCT in 18 patients with IPF. We could not overestimated these results because are based only on a limited number of subjects and on a correlation factor of – 0.47; it should be supported by a follow-up study in order to investigate if the clearance of 99m-DTPA can actually predict the clinical course of IPF. Furthermore, a recent study demonstrated that clearance of 99m-DTPA, although abnormal in all subjects in presentation, was not a predictor of disease progression in IPF patients (Mura M, et al. Can Respir J 2004; 11: 477-9). Additionally, Mogulkoc et coworkers showed that the predictive value of the aforementioned technique (in terms of survival) was lower than that of total lung capacity and DLCO, and the clearance values did not correlate with the HRCT score (Mogulkoc N, et al. Thorax 2001; 56: 916-23).

In summary, we believe that at the moment there are not sufficient evidences to recommend the implementation of DTPA scan in the follow-up of IPF patients. Further studies in large scale of patients are needed to define the role of this technique in pulmonary fibrosis.

Major Compulsory Revisions

The definitions of mild, moderate, severe needs clarification. What is the source of these categories. How are they defined. The HRCT scoring system is not well defined. I advise
using Kazerooni et al. The references for the scoring used are heterogenous. I am unsure that TID is a specific concept derived from the references given.

REPLY: Indeed the description of HRCT scoring was not very clear. By "... the level of 5%..." it is meant that the nearest estimation of extent of disease at each level included also the half of tenths. This definitely allows a more detailed approximation than an evaluation at the nearest 10%, and has been used in several papers that correlate disease extent at HRCT with functional indices (mentioned at the material and methods section of the paper).

The percentages represent extent of involvement. Their maximum and minimum possible scores range from 0 to 100%. A 50% score at a particular level means that half of the parenchyma seen at this slice has findings of interstitial lung disease. The TID (total interstitial disease score) is an overall score of interstitial involvement and is calculated by adding the individual scores of the five levels evaluated and then dividing it by five. A patient with scores 10%, 10%, 15%, 20%, 30%, and 45% at the five evaluated levels will have a TID of 26% (10+10+15+20+30+45 divided by 5).

The classification of severity of disease in mild moderate and severe is somehow arbitrarily made based on the TID obtained from the above calculations. Patients with TID values from 0 to 20% were considered mild (grade 1), those with 21 to 40% as moderate (grade 2) and those with TID >40% as severe (grade 3).

In addition, we have enclosed more precise references about the methodology of the HRCT scoring in the revised manuscript, according to your suggestion.

Again, thank you very much for your constructive comments

On behalf of the authors,
Professor Demosthenes Bouros