Reviewer’s report

Title: Diagnostic yield and risk/benefit analysis of trans-bronchial lung cryobiopsy in diffuse parenchymal lung diseases: a large cohort of 699 patients

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Reviewer: Francesco Varone

Reviewer's report:

This is a well written retrospective study. The argument, i.e. the diagnostic value of trans-bronchial lung cryobiopsy in the context of diffuse parenchymal lung diseases, is extremely timely, and was not addressed in the recently published guidelines on IPF diagnosis (Raghu G, Remy-Jardin M, et al AJRCCM 2018). However, important considerations regarding study design and conclusions should be made.

Major comments:

Page 4, lines 78-81: It is unclear whether the two pathologist who reviewed the second series of TBLC were blinded or not to clinical and radiological data.

It seems that in the first series the Authors applied a method used in an already published paper of the same group (see Tomassetti S et al AJRCCM 2016);

If the methodology used for the second series presented in this paper is different (e.g real-life approach in the context of a multidisciplinary diagnosis with all the available data) this must be stated in the manuscript. Moreover, this can also influence results and conclusions of the present paper. I suggest that a new table with data/results coming from the second series be presented in the manuscript.

Page 12, lines 290-291: This statement is completely arbitrary, is markedly different from the recently published guidelines on IPF diagnosis (AJRCCM 2018), and should therefore be removed.

Minor comments

Page 5, Lines 107-110: It would be useful to know the level of confidence of the pathologists, in particular for UIP pattern.
Page 11, lines 267-268 It is unclear whether patients with a diagnosis of CTD-ILD did receive only a pathological diagnosis, or if the diagnosis was based on clinical/laboratory findings and rheumatologic consultation.

General comment

It is a pity that, given the large number of patients, the diagnostic yield of diagnosis obtained by trans-bronchial lung cryobiopsy was non plotted against clinically meaningful measures, as mortality or disease progression. This might have strengthened the results of the present study.

**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.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
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Acceptable

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