Peer Review File

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Reviewer A:

Comment: The authors, who have sufficient experience of ILD in the UK, reviewed SLB for ILD using snowball sampling and the realist review method. This review paper is well written and and very concise. My comments and questions are given below.

Although the authors show that failing a definite diagnosis from the initial panel, further investigative options (BAL, TBB, cryobiopsy, and SLB) would be needed, they do not indicate which procedure would be preferable for patients with ILD. The risks and benefits are compared among these procedures in Table 1, but there is no indication for the strategy to choose which investigative option is better for each patient. Thus, how these invasive diagnostic procedure are selected should be argued in discussion, based on the information from guidelines and previous papers, and the knowledge and experience in the authors' hospital.

Reply: We have added a paragraph to this effect. Thank you for the feedback!

Reviewer B:

Comment 1: It is a great review by Annemarie Brunswicker et al focusing on indications and technics for SLB in the field of ILD.
I think it is well written, and the question asked is more than clinically relevant and is well discussed by the authors. However I have several comment to share and would ask for revisions before publication.

Major revision
Modern and robust data are accumulating regarding safety and efficacy of endoscopic lung cryobiopsies for ILD diagnostic and is now available as a potential way to obtain lung histology as supported by recent 2022 IPF guidelines. This review should precisely discuss the advantage and disadvantage of SLB in comparison .

Reply 1: Thank you very much for your detailed feedback.
Unfortunately, the line numbering in our document does not seem to align with the line counts referred to in this review, which made addressing some of the comments difficult.
We have tried our best to address the suggestions, however we could not always work

out which exact sentence/line of the paper has been referred to. Please do let us know of any discrepancies, which would have arisen due to differences in line count.

Minor comments
Comment 2: Title:
I suggest authors add “for interstitial lung disease” for more clarity in the title
Reply 2: Thank you – we have added this.

Comment 3: I suggest to change the ref 3 for the 2022 IPF guidelines update that is more suitable for describing IPF course
Reply 3: We have changed this reference accordingly.

Comment 4: Line 59-61: I suggest to delete the sentence regarding immunosuppression since it has been completely abandoned since more than ten years.
Reply 4: Thank you for highlighting this point – sentence taken out.

Comment 5: Line 71, Paragraph: I think the authors highlight with great precision this important consideration and I thank them for this point that is very important when dealing with ILD and SLB.
Reply 5: Thank you for your feedback!

Comment 6: Line 81, I suggest to had the great paper from AJRCCM from Cottin et al (2021 or 2022) dealing with IPF confidence in diagnosis
Reply 6: We have added this reference.

Comment 7: Line 107, UK and USA, not only…
Reply 7: Thank you for this comment – we acknowledge that other centres might have a similar approach globally, however it is outside our expertise to comment on pathways elsewhere and would probably be too much to explore for the purpose of this review.

Comment 8: Line 117, I think that this >90%may be possible in highly expert center but absolutely need to be modulated and presented with its high variability in literature according to center, and diagnostic criterias
Reply 8: We have added to the sentence to reflect this.

Comment 9: Line 120: cf above, major comment, I think that cryo should be treated separately in a fully described paragraph.
Reply 9: We have added a new paragraph for TBLC. The change in guidelines only occurred after we first submitted the paper - thank you very much for highlighting this important point.

Comment 10: Line 125: concerning tbb: I would suggest to insist more on its very

rare indication as supported by recent guidelines in the field of ILD considering high risk and low rentability except maybe sarcoidosis for example.
Reply 10: We have amended the paragraph to highlight this.

Comment 11: Line 150: Please provide range according to studies more than one single study considering large disparity according to studies
Reply 11: We are unsure what this refers to – where relevant we have cited several studies.

Comment 12: Line 173: Please add a recent ref Pastre et al Annals of ATS 2021 and the complications rate found in this paper (global and in the elective pop)
Reply 12: We have added a sentence to mention these findings.

Comment 13: Line 179: please describe range of complication in the literature more than in a single study.
Reply 13: We have included the confidence interval ranges of the complications (assuming that was what you meant)

Comment 14: Line 194-220: I would suggest to add a small paragraph on acute exacerbation after SLB, and possibly detail of anesthetic and peri operative technics that may be associated with lower risk (avoid hyperoxia and overflluid rescucitation during procedure, prompt or immediate mobility and physio after surgery…)
Reply 14: While these are important, it is not the main focus of the paper, which instead centres around decision-making around diagnostic pathways. We have signposted to relevant ERAS and clinical guidelines instead, in order not to overload the paper with what could potentially be a separate review!

Comment 15: Line 235, please provide ref
Reply 15: Our line count does not seem to align with yours. I am not entirely sure where this is referring to?

Comment 16: Paragraph 238: please highlight the fact that parameters in this scoring system may seems no longer appropriate
Reply 16: We assume you are referring to the aggregate risk score by Fibla et al? If so, we have highlighted that it is not in practical use due to lack of validity.

Reviewer C:

Comment 1: It is an excellent text, with a thorough and didactic review, illustrating both an extensive literature review and the experience (vision) of the authors.
Two importante (although not major) issues, however, should be clarified, in my

opinion, for eventual acceptance for publication.
-First, the scope of the article itself (including the title). This is a review of surgical lung biopsy in patients with interstitial diseases, in an elective status. Therefore, nodule biopsies, or hospitalized patients with acute diseases / respiratory failure / mechanical ventilation, or acute infiltrates in immunosuppressed patients, or other situations are excluded. This is reasonably described in the text, but this should be further clarified in the title for the guidance of future readers and researchers. Therefore, I suggest that the title includes "... on lung biopsy in interstitial lung diseases: who...".
Reply 1: Thank you for outlining this – we have changed the title accordingly.

Comment 2: Second, I think that among the justifications and benefits for performing SLB in patients with ILD is in the prognostic assessment (and prediction of therapeutic response to certain therapeutic agents), particularly in idiopathic pulmonary fibrosis. This was placed by the authors in a figure (Figure 2), but I did not find it in the text itself. This is not only about defining prognosis by determining a more "benign" or "poor" diagnosis (disease A or B), but defining the severity stratification (or prediction of therapeutic response) within a given disease based on histopathology. Although controversial (or precisely because of this), it is worth at least mentioning the topic (Raghu G, et al, for the ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med. 2011; 183 (6): 788-824).
Again, congratulations on the article!
Reply 2: Thank you for this suggestion– we have added a short paragraph at the beginning of the discussion to address this issue.