Responses to Reviewers Comments

Please see below response in black.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: ILD is a heterogeneous disorder affecting the lungs. AE-ILD epresent an acute,frequent and often highly morbid event in the disease course of ILD patients. Admission in the intensive care unit (ICU) is very common. Management can be viewed as a multi-faceted approach that is mainly comprised of supportive care for respiratory failure. Specific comments are presented below.

1.In Definition, the authors seem to have repeated statements, such as "but defined AE-IPF as an "acute, clinically significant respiratory deterioration characterized by evidence of new widespread alveolar abnormality typically less than one month's duration." Currently, an acute exacerbation (AE) of IPF is defined as an acute, clinically significant respiratory deterioration characterized by evidence of new widespread alveolar abnormality typically less than one-month duration".

We sincerely appreciate the important feedback you provided, as it has helped us improve the clarity and coherence of our manuscript. Following your suggestions, we have made significant changes to streamline the content and ensure that our ideas are presented in a concise and effective manner. We believe that these revisions have greatly enhanced the overall quality of the paper, and we are grateful for your valuable input.

2. In Triggers, the authors discuss differentiate between rapid deterioration (RD) and AE of ILD. How does progressive pulmonary fibrosis (PPF), a new concept, differ from AE-ILD?

Reviewer has highlighted an important point. Currently it's difficult to precisely differentiate AE-ILD from PPF and we have to rely on clinical history and presentation. As summarized in the paper, using a multimodality approach involving an ILD pulmonologist, might help differentiate and manage these conditions.

3. "Finally, there is the added advantage of the patient able to eat and communicate with HFNC versus IMV." Are these advantages of HFNC compared to IMV or NIV?

Thank you for bringing this to our attention. We have clarified this point in the manuscript. It is worth noting that both high-flow nasal cannula (HFNC) and bilevel positive airway pressure (BiPAP) are types of noninvasive ventilation (NIV). One of the advantages of using NIV modalities such as HFNC and BiPAP is that patients are able to eat and talk to the extent that they can tolerate, unlike with endotracheal intubation and invasive mechanical ventilation (IMV).

4.Reference: there is a very relevant publication recently, how does your review compare to this one? Charokopos A, Moua T, Ryu JH, Smischney NJ. Acute exacerbation of interstitial lung disease in the intensive care unit. World J Crit Care Med. 2022 Jan 9;11(1):22-32.

Charokopos et al have done an awesome job in this review. Our paper summarizes the diagnostic and treatment modalities, as well as the dilemmas faced by physicians when managing acute exacerbation of interstitial lung disease (AE-ILD). Although the basic concept is similar to the mentioned paper, our perspective is unique and provides vital information specifically targeted to busy ICU physicians.

5.The authors show two Fig.3?

Thank you for bringing this clerical mistake to our attention. We have revised the manuscript to correct the error.

6.In Table 1, the authors show errors in details and unclear abbreviations, such as HHFNC and ECLS.

Authors are thankful for the feedback and relevant changes to Figure have been made.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: I read with great interest the manuscript entitled "Acute Exacerbation of Interstitial Lung Disease in the ICU: Principles of Diagnostic Evaluation and Management". The manuscript intends to discuss the management of AE-ILD. However, there are certain issues which I would like to highlight

1. There are certain grammatical and typographical errors which need correction, especially in the Abstract and the core tip.

Thank you for providing feedback on our manuscript. We appreciate your input and have made the necessary revisions to improve the clarity and accuracy of our work. We strive to ensure that our manuscript is of the highest quality and your feedback has been instrumental in achieving this goal.

We recognize that the topic of AE-ILD is complex and that there is limited clinical data available to formulate comprehensive treatment guidelines. However, we believe that our manuscript provides valuable insights for intensivists encountering these patients in the ICU setting.

In particular, we emphasize the importance of a multimodality team approach in the timely diagnosis and management of AE-ILD. We believe that this approach can improve both morbidity and mortality outcomes for these patients. Additionally, we discuss the appropriate treatment options for patients with irreversible end-stage respiratory failure, including lung transplantation and palliative care. We appreciate

your contribution to our work and hope that our revised manuscript meets the standards and expectations of the readership.

2. Introduction: "The idiopathic ILDs can be further distilled into 3 compartments:.." Pls rephrase this line.

Thanks for the input appropriate changes have been made.

3. Introduction: 2 paras have been dedicated to CT scan in the introduction. It may be put in the workup where again CT scan has been discussed in detail.

Thank you for your input, and we have implemented the appropriate changes to the manuscript.

4. Triggers: "The incidence of AE-IPF is up to 15% per year, depending on the cohort studied. However, in several recent IPF trials, there was a reported incidence of 2-15% per year" Pls rephrase this sentence.

The authors are grateful for the feedback provided, and have incorporated the suggested revisions into the manuscript.

5. ECMO: Please rephrase this sentence "In summary, outside of patients with a clearly reversible cause (e.g., infection or pulmonary embolism) or those suitable for transplant, ECMO should not be offered, given the associated morbidity and economic implications".

Thanks for the input appropriate changes have been made in the manuscript.

1. Lung transplant: Please rephrase this sentence "Pre-transplant IMV and ECMO have known risk factors for adverse post-transplant outcomes…"

Thank you for bringing the errors to our attention. We have revised the manuscript to depict these changes.

7. Classification of DPLD has also been labelled as “Table 1”

Thanks for the input appropriate changes have been made.

8. None of the tables have been mentioned in the text.

Thank you for your input, we have made the necessary changes to improve the manuscript.

9. Several words are repeated throughout the manuscript even though their short forms were introduced when they were first mentioned.

Thanks for pointing out the errors, manuscript was revised to correct any duplications.

10. Overall, this seems to be **narrative review rather than a clinical review**. Would suggest adding some clinical evidence, literature review and provide some suggestions for managing these patients based on the data.

We appreciate the authors' observation. The management of acute exacerbation of interstitial lung disease (AE-ILD) is a complex topic with limited clinical data available to guide evidence-based recommendations. Future studies are needed to develop comprehensive treatment guidelines for AE-ILD, some of which are already underway as mentioned in the manuscript. As a narrative review, our paper provides clinical applications for intensivists who may encounter these patients.

11. Adding a table on the available therapies, including dosage, indications and side effects, may be helpful for the reader.

Thanks for the input appropriate changes have been made. Figure 2 depicts a flowsheet to guide management plan of AE-ILD.