

## Reply to the Peer-review report of Manuscript NO: 73807

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Reviewer #1: This paper is well written. Please investigate the relationship between this score and the time of onset of ARDS.

Answer: We are very grateful for your insightful comments regarding our manuscript. We believe that it's very important to investigate the relationship between our score and the time of onset of ARDS. Unfortunately, the onset time-point of ARDS was not involved in our previous study design, and it would be very hard to replenish any added item in a multi-center study. For this reason, we couldn't clarify this question by now. We apologize for our ill-considered design, and we recognize this limitation should be mentioned in the paper. So we added following sentences to address your concerns: "Moreover, the exact onset time of ARDS was not involved, so new model only predicts the risk of ARDS during the whole admission (range from 7 to 15 days) using the scores gained within 24 h of admission. It might not be very appropriate, and new model couldn't tell the clinicians when they should prepare for the possible onset of ARDS neither. Further studies are needed to verify the value of new models on a dynamic time-scale" (Please see Page 14 of the revised manuscript, lines 383-388). We would like to thank the referee again for taking the time to review our manuscript.

Reviewer #2: I believe it would be interesting to inform an average of ventilatory patterns, since they interfere with pro-inflammatory mediators. Just a suggestion.

Answer: Thank you for your insightful comments. We agree with you that it would be very useful to inform an average of ventilatory patterns. However, detailed information was not involved during data collection, so we couldn't provide it in current manuscript. We apologize for the defect of study design, and we added following sentences to address your concerns: "It must be mentioned that mechanical ventilation will attenuate systemic inflammation of ARDS and the effect varies with patterns<sup>[1]</sup>. It's unavoidable that new score to predict ARDS will also be affected. Unfortunately, detailed information of mechanical ventilation was not collected in this

study, and further researches are needed to investigate the influence of different ventilatory patterns on new models” (Please see Page 14 of the revised manuscript, lines 397-402). Thank you very much for taking the time to review our manuscript.

1 Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, Herridge M, Randolph AG, Calfee CS. Acute respiratory distress syndrome. *Nat Rev Dis Primers* 2019; **5**(1): 18 [PMID: 30872586 PMID: PMC6709677 DOI: 10.1038/s41572-019-0069-0]