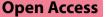
MATTERS ARISING



Time-dependent effect of prone position in ARDS: considerations for future research

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To the Editor

We have read the article by Yuan et al. [1] with great interest, where they indicated that prone position significantly reduced ventilation/perfusion (V/Q) mismatch in patients with early ARDS, while it increased V/Q mismatch in persistent ARDS patients. However, there are several factors that might influence the reported findings:

Firstly, it is important to consider that the effect of prone position is time-dependent. Instead of defining a 20% improvement in PaO₂/FiO₂ at 2 h as a responder, it would be more appropriate to compare PaO_2/FiO_2 at the end of the prone position to the baseline. PP has a timely gravity effect on the change of ventilation, and also takes time to gradually open up collapsed or consolidated alveoli and drainage secretion. Additionally, previous studies have shown that PaO_2/FiO_2 increases during the first 3 h of PP, but further improvement in PaO₂/FiO₂ occurs in later stages due to increased ventilation and blood flow then more matched regions [2]. Therefore, we believe that using the PaO₂/FiO₂ at 2 h in the PP may not accurately define the reactivity of PP at 12 h. In the study, out of the 24 patients with persistent ARDS, 23 (95.8%) had moderate ARDS. Although the Shunt-EIT% (including

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ventral and dorsal) and Total unmatched units increased significantly, there was no statistical difference in the PaO_2/FiO_2 of these patients after 12-h PP (Table 2). There is a lack of information on changes in matching or oxygenation during the 12-h period. It would be valuable to understand whether there is a peak effect of PP and its timing, as this could provide guidance for implementing this intervention. Therefore, further investigations which assess the time-dependent effect of PP in ARDS of different severity and time stage are warranted.

Secondly, this study defined ARDS days as starting from the initiation of non-invasive or invasive ventilation until the first PP. The initiation of non-invasive or invasive ventilation alone cannot be classified as ARDS without the support of imaging results at the time and the exclusion of heart failure. Figure E2 illustrates that the initial PaO₂/FiO₂ values were around 200 mmHg during the first two days of non-invasive/invasive use but decreased thereafter with a downward trend. There might have been a delay for intubation or PP in some persistent ARDS cases where it took seven days before initiating PP. Therefore, it is possible that the effectiveness of PP is not solely attributed to persistent ARDS, but also influenced by underlying pathological mechanisms, such as excessive respiratory drive leading to patient self-inflicted lung injury (P-SILI) [3, 4] or VILI [5], and aggravated basic disease. Moreover, the impact of early PP on the progression of ARDS necessitates further investigation.

Considering an early attempt at awake PP might also be reasonable. For persistent ARDS cases with suboptimal improvements in oxygenation despite PP, it is worth considering alternative approaches. Could a extended duration of PP or combining PP with inhaled nitric oxide (iNO) yield better results? Further research is needed to



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address these questions and explore how it can lead to less shunting and facilitate efficient gas exchange.

Abbreviations

- ARDS
 Acute respiratory distress syndrome

 V/Q
 Ventilation/perfusion

 PP
 Prone position

 EIT
 Electrical impedance tomography

 P-SILI
 Patient self-inflicted lung injury
- iNO Inhaled nitric oxide

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YW wrote the main manuscript text. All authors reviewed relevant literatures, discussed about the topic, and reviewed the manuscript. All authors approved the manuscript.

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