



## Reply to: Effect of prone positioning without mechanical ventilation in COVID-19 patients with acute respiratory failure

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Reply to Yanfei Shen and co-workers:

We have read the letter by Yanfei Shen and co-workers, and appreciate their interest in our study of awake prone positioning (APP) in non-intubated patients with acute hypoxaemic respiratory failure (AHRF) due to coronavirus disease 2019 (COVID-19). We would like to add a few comments to their purposeful remarks.

Yanfei Shen and co-workers compare the results of our observational study [1] to those of two different clinical trials. The trial by QIAN *et al.* [2] has been criticised due to the short time that patients remained in the APP (4.2 h per day) which can be associated with treatment failure when patients remain in the prone position for less than 8 h per day, and for disparities in patients among groups who had no-resuscitation orders and were thus not offered advanced life support [3–6]. Similarly, in the study by ALHAZZANI *et al.* [7], patients were only exposed to 5 h per day APP despite the investigators' intentions to reach >8 h per day, which could explain the lack of benefit in this trial as well.

We agree with Yanfei Shen and co-workers in that APP could possibly benefit only patients with mild-to-moderate AHRF, especially those with an estimated peripheral arterial oxygen saturation to inspiratory oxygen fraction ratio >150. Adding to their theory, we believe that APP failure in patients with severe AHRF could be the cause of operational ventilations that are associated with pressure self-inflicted lung injury, which implies swings in transpulmonary pressure, increasing volume in aerated compartments, abnormal increases in transvascular pressure, pulmonary oedema, the pendelluft phenomenon, and diaphragm injury [8].

It is worth remembering that the generation of knowledge to reach conclusions regarding the benefits or lack thereof from a medical intervention can be lengthy. In the case of the prone position for unconscious patients under invasive mechanical ventilation, it took more than 13 years until benefits in mortality were undisputed [9], since results from studies prior to the PROSEVA trial [10] had been uncertain. During the COVID-19 pandemic, an impressive amount of varying quality observational and experimental studies evaluating APP to prevent intubation or death were generated. Furthermore, in 2 years of the pandemic, 10 systematic reviews and meta-analyses on the topic have been published with conflicting results, more often showing possible benefits from this intervention [11].

Undoubtedly, several questions remain to be answered regarding APP for AHRF. We have chosen the following questions which we believe are relevant to be considered when envisioning new studies on the topic:

- 1) How much time should a patient remain in APP per day?
- 2) How do multiple short intervals *versus* more prolonged intervals affect the efficacy of APP when these are equal in terms of the daily dose?
- 3) Could APP work better in patients who have not progressed to require supplementary oxygen through high-flow oxygen devices?
- 4) What are the other (possible) factors which predict which patients may benefit from APP or not?

In the meanwhile, we consider that APP has been shown to be a safe intervention which is highly reproducible, of low cost, and with still undetermined benefits for patients with AHRF. Taking this into









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**Several questions on the efficacy of awake prone positioning for hypoxaemic respiratory failure remain unanswered. Research targeting those questions is needed.** <https://bit.ly/3xmbNPP>

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account, we are certain that it is worth continuing to study it. For the prior outlined reasons, we as clinicians still encourage conscious patients with AHRF to remain in the prone position if tolerated and have a compromise to continue studying this intervention to attempt to solve some of the still unanswered questions.

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