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Prone positioning might reduce the need for intubation in people with severe COVID-19

We applaud the recent Article in *The Lancet Respiratory Medicine* by Stephen Ehrmann and colleagues¹ regarding awake prone positioning in patients with COVID-19. Safely avoiding endotracheal intubation is important for patient wellbeing and resource allocation. The findings of this study raise important questions.

Five participants withdrew consent after randomisation and were not included in the intention-to-treat analysis, which is relevant given the fragility index of 5 for the primary outcome. If both control patients avoided intubation or death and all three awake prone positioning patients were intubated or died, this result would have yielded non-significance for the primary outcome. 44 (8%) of 564 patients in the overall awake prone positioning group had a do-not-intubate order. If five awake prone positioning patients were not intubated but did not die during the study period, this could have nullified statistical significance.

As the authors acknowledged, the Mexican trial results drove the positive outcome of the study. As the Mexican

trial had the largest study population and effect, this trial warrants further discussion, particularly since the trial joined after a standardised protocol was implemented. Nearly 80% of the Mexican awake prone positioning patients were outside the intensive care unit, where access to endotracheal intubation was presumably restricted. Meanwhile the French and American trials had more than 80% of awake prone positioning patients in the intensive care unit. The Mexican protocol diagram shows a markedly different SpO₂ threshold (SpO₂ ≤80%) for intubation compared with the other trials. Presumably this protocol variation could have resulted in fewer intubations and thus statistical non-significance. We recommend use of objective intubation criteria to the extent possible, particularly in the context of an unmasked study.

Remarkably, the baseline ratio of SpO₂:FiO₂ (135) in the Mexican awake prone positioning group was 17 points lower than the SpO₂:FiO₂ in any of the other trials. This SpO₂:FiO₂ ratio corresponds to a PaO₂:FiO₂ ratio of 85 if imputed linearly.² Not only is this value consistent with severe acute respiratory distress syndrome (ARDS), but it is also below the intubation threshold (PaO₂:FiO₂ <100) of the French trial where prone positioning would have been declared a failure.

Although some data suggest that prone position-induced improvements in gas exchange do not predict mortality in ARDS in ventilated patients,³ it would be interesting to test prospectively if prone positioning in non-intubated patients with COVID-19⁴ prevents intubation or improves mortality. Either way, we believe, based on these new data and previous prone positioning trials,⁵ that prone positioning probably protects the lung mechanically, particularly when implemented early in disease and when sustained for long periods of time each day.

We declare no competing interests.

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