Awake Prone Positioning in COVID-19: Signal or Noise?

To the Editor  In their article, Dr Qian and colleagues\(^1\) reported the results of a trial comparing awake prone positioning (APP) with usual care in nonintubated adults with COVID-19--induced hypoxemia. Although it provides insights into the nuances and perils of APP, their findings contrast with the results of a recent metatrial in which lower intubation rates were observed with APP.\(^2\)

The authors’ pragmatic approach\(^1\) provides gross answers about the universal efficacy of APP. However, it goes hand-in-hand with a decrease in the attributable risk of APP and prognostic enrichment of the sample. In their study, two-thirds of patients had low-flow oxygen requirements, whereas the metatrial by Ehrmann and colleagues enrolled only patients with high-flow oxygen.\(^2\) The former did not find benefit, whereas the latter did. It is inevitable to wonder if we are repeating the story of prone positioning in mechanical ventilation: not enriching for disease severity and thereby losing the signal of benefit.\(^3\)

The outcome used by the authors\(^1\) further increases the background noise and perhaps, attenuates the signal. By using the World Health Organization’s COVID-19 ordinal outcome scale, they diluted the clinical end point for which APP was implemented in the first place, ie, reducing the need for intubation. Both the metatrial and the cumulative analysis of observational studies\(^4,5\) suggest that the benefit of APP resides in its association with a reduced need for intubation in patients requiring high-flow oxygen.

Dose matters. We have learned this from trials in prone positioning.\(^3\) The growing body of evidence hints that this may be the case with APP. In the trial by Dr Qian and colleagues,\(^1\) the short APP median time of 4.2 hours per day was ineffective and perhaps even harmful. However, in the metatrial by Ehrmann and colleagues, prolonged APP duration reduced intubation rates and treatment failure with no signal for harm.\(^2\) Of note, the outcomes were driven by the center that achieved longer APP sessions. Either APP is dose-dependent, with minimal threshold for efficacy, or patients who tolerate prolonged APP are inherently less likely to experience worsening of their condition.

Certainly, the study by Dr Qian and colleagues\(^1\) discourages the widespread use of APP in every degree of oxygen requirement and suggests that, in the wrong patient, it may lead to escalated level of care. However, considering the cumulative evidence of benefit in patients requiring high-flow oxygen, we should focus on studying this subgroup. Our research agenda should move toward promptly identifying APP response and failure (validating/creating prediction tools) and the ideal APP dose and factors that may improve adherence to the intervention.

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