



Awake prone positioning for patients with covid-19

It's a matter of time

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Awake prone positioning is thought to improve clinical outcomes in patients with covid-19 by modulating lung mechanics during progressive hypoxaemic respiratory failure.^{1,2} The intervention is attractive because of its perceived simplicity, with evidence of benefit in patients with acute respiratory distress syndrome who need invasive mechanical ventilation. However, data to inform its use in patients with covid-19, particularly those not requiring mechanical ventilation, are scarce.^{3,4}

Randomised evidence from 2021 looked promising. In a meta-trial combining data from six open label superiority trials of patients requiring high flow nasal oxygen for covid-19, Ehrmann and colleagues found that awake prone positioning significantly reduced the risk of intubation or death compared with standard care (223 (40%) outcome events in the prone cohort versus 257 (46%) in the standard care cohort; relative risk 0.86, 95% confidence interval 0.75 to 0.98).⁵

Now a linked *BMJ* paper by Fralick and colleagues (doi:10.1136/bmj-2021-068585) reports findings from a new pragmatic randomised controlled trial of awake prone positioning in patients admitted to hospital with covid-19 across 15 North American centres (COVID-PRONE).⁶ A total of 257 participants requiring supplemental oxygen were assigned to prone positioning or standard care. The composite primary outcome was death, invasive mechanical ventilation, or worsening respiratory failure requiring at least 60% fraction of inspired oxygen. By contrast to previous findings, COVID-PRONE found no differences in the primary outcome between the intervention group (18 (14%) events) and the control group (17 (14%) events) (odds ratio 0.92, 95% confidence interval 0.44 to 1.92).

How can the discrepancy be explained? Firstly, participants in the meta-trial were managed awake and prone for a median of five hours daily, twice as long as participants in COVID-PRONE. Despite the authors' best efforts (COVID-PRONE aimed for 16 hours a day prone and went through eight iterations to try to improve adherence), the median daily duration of prone positioning in the first 72 hours was 2.5 hours in the intervention group (with no proning at all beyond 72 hours) compared with 0 hours in the control group. Therefore, one of this trial's key findings was that, in routine clinical settings, awake prone positioning is difficult for patients to tolerate for long enough to improve outcomes. In the meta-trial, the largest contributor to overall benefit was a Mexican sub-study, in which long durations of prone positioning were achieved

(8.6 hours per day), resulting in a relative risk reduction of 22%.

Unlike sedated patients, awake patients with covid-19 are uncomfortable and in pain. Patient author DP was admitted to intensive care early in the pandemic and recalled breathing as though his lungs "were filled with shattered glass." Combined with febrile episodes, fatigue, and the mental distress caused by an acute life threatening illness, lying face down for prolonged periods while awake can be extremely difficult. The Mexican sub-study of the meta-trial may have achieved better adherence and outcomes because an intensive care specialist was constantly available to encourage patients and clinical teams to persevere with prone positioning. This resource would be unavailable in most standard healthcare settings. Even in an intensive care unit with one-to-one nursing, awake prone positioning can be poorly tolerated.⁷

Secondly, differences in disease severity existed between participants in COVID-PRONE and previous trials. Only 4% of patients in COVID-PRONE required high flow nasal oxygen at baseline, whereas the meta-trial predominantly enrolled sicker patients already needing non-invasive respiratory support. Rates of mortality and intubation varied substantially between the trials—1% versus 22.2% and 4% versus 36.4%, respectively. These differences likely contribute to the discrepancies in the findings.

Duration of covid-19 infection is intrinsically linked to its severity, so both may be modifiers of the efficacy of prone positioning.⁸ In patients with early or mild disease, pulmonary physiology is probably insufficiently compromised for prone positioning to make a difference to outcomes through its effects on transpulmonary pressure distribution, lung compression, and ventilation-perfusion mismatching. During advanced, severe disease, however, prone positioning could help to reduce regional alveolar hyperinflation associated with raised positive end expiratory pressure, especially in patients requiring non-invasive respiratory support.

Fralick and colleagues' new trial, together with previous trials, shows that both duration and timing of awake prone positioning are important determinants of its efficacy in patients with covid-19. Future studies must focus on finding optimal means of maintaining awake prone positioning in the care of severe, likely late stage covid-19. Patient and public involvement will be crucial to ensure that appropriate attention is paid to comfort and acceptability in the design and evaluation of complex interventions to enable awake prone positioning.

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Awake prone positioning can still work, but timing and duration are fundamental determinants of efficacy as an intervention for progressive hypoxaemic respiratory failure in patients with covid-19.

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