Awake prone positioning in COVID-19

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In the absence of effective targeted therapies for COVID-19, optimisation of supportive care is essential. Lung injury with features of acute respiratory distress syndrome (ARDS) appears to be the principal characteristic of severe acute respiratory syndrome coronavirus 2 infection.[1] Recent guidance by the UK Intensive Care Society (ICS) advocates awake prone positioning to become standard of care for suspected or confirmed COVID-19, in patients requiring an FiO_2 ≥28%0.[2] These recommendations are extrapolated from physiological principles and clinical evidence obtained in a distinct study population—patients with severe ARDS undergoing invasive mechanical ventilation (IMV).

The physiological rationale behind prone positioning in typical ARDS is to reduce ventilation/perfusion mismatching, hypoxaemia and shunting.[2] Prone positioning decreases the pleural pressure gradient between dependent and non-dependent lung regions as a result of gravitational effects and conformational shape matching of the lung to the chest cavity. This is believed to generate more homogenous lung aeration and strain distribution, thus enhancing recruitment of dorsal lung units.[3] Prone positioning does not appear to alter regional distribution of pulmonary blood flow, with perfusion predominating towards dorsal lung aspects due to non-gravitational factors.[4] With improvements in ventilatory homogeneity and relatively constant perfusion patterns, a subsequent reduction in shunting is observed.[5] The use of positive end-expiratory pressure via non-invasive ventilation (NIV) or CPAP in the management of ARDS is beneficial by preventing alveolar de-recruitment but may also result in overdistension of previously well-ventilated alveoli.[6 7] Similarly, spontaneously breathing patients in acute hypoxaemic respiratory failure can generate high respiratory drives and forceful inspiratory efforts that lead to lung injury reminiscent of ventilator-induced lung injury.[8] Prone positioning in these patients and in combination with NIV/CPAP may help to mitigate this detrimental effect in part by reducing regional hyperinflation.[9]

Prone positioning is an established evidence-based practice in patients with typical ARDS undergoing IMV, but limited evidence exists in non-ventilated awake patients. In a multicentre, randomised controlled trial of patients with severe ARDS receiving IMV, prone positioning halved 28-day mortality rates (16% vs 32.8%, $p<0.001$) with no additional complications.[10] Meta-analyses suggest that early prone positioning for 12–16 hours/day combined with low tidal volume IMV reduces mortality in severe hypoxic respiratory failure.[11–13]

Presently, no published trials investigate the effectiveness of prone positioning in awake patients with typical ARDS. Evidence in awake prone positioning is limited to case series and small observational studies with heterogenous approaches to non-invasive respiratory support. These reports demonstrated short-term improvements in oxygen requirements (PaO_2) and demand (FiO_2) with no harm to patients.[14–16] Valter *et al* applied prone positioning to four patients with indications for IMV and found rapid improvements in PaO_2—all patients avoided IMV and tolerated prone positioning well.[14] In an observational study of 15 patients receiving non-invasive respiratory support for acute hypoxaemic respiratory failure, repeated prone positioning led to transient but substantial improvements in oxygenation.[15] In a prospective observational study of 20 patients receiving non-invasive ventilation for moderate-to-severe ARDS, PaO_2/FiO_2 ratio increased by 25–35 mm Hg following awake prone positioning; but 78% of participants with severe ARDS eventually required IMV, and therefore awake prone positioning should not delay the use of IMV when indicated.[16]

The notion of applying evidence generated in typical ARDS universally to patients with COVID-19 is challenged by Gattinoni *et al* based on their analysis of 150 patients.[17] They hypothesise lung injury in COVID-19 to encompass a time-dependent spectrum of disease with variable patterns of lung pathology and heterogenous responses to prone positioning.[17] In early phases of COVID-19 pneumonitis, lung compliance is proposed to be high, recruitability minimal and hypoxaemia predominantly driven by impaired regulation of pulmonary perfusion patterns.[17] Awake prone positioning here could temporarily improve ventilation/perfusion mismatch, but sustained benefits in highly compliant lungs are unlikely.[17] With disease progression, COVID-19 pneumonitis is thought to gradually start behaving like typical ARDS, demonstrating lower compliance and higher recruitability with a more favourable long-term response to prone positioning. It is suggested that phases of COVID-19 pneumonitis may be distinguished prior to intubation using CT measurement of lung weight, gas volume and proportion of non-aerated tissue, although additional large studies are required to validate this diagnostic modality.[17] During a pandemic, application of CT scanning to all patients with COVID-19 for this purpose is unlikely to be feasible and will bear future risks related to radiation exposure. Further work to confirm or refute the hypothesis put forward by Gattinoni *et al* is needed. Estimating the frequency and speed of phase transition as well as identifying pragmatic surrogate markers to predict disease phase may be useful in selecting those who could benefit the most from awake prone positioning.

Furthermore, the minimum duration requirements for maintaining the prone position in awake patients to engender clinically meaningful benefits remain undefined. Durations comparable to those necessary for patients undergoing IMV (12–16 hours/day) may be difficult to achieve. For instance, the longest duration of prone positioning achieved in observational studies of awake patients was 8 hours. Improved lung secretion drainage under gravitational forces and increased coughing following prone positioning may contribute to viral contamination of the patient environment, necessitating the

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use of adequate personal protective equipment during patient contact.

In summary, awake prone positioning appears to be safe and may slow the respiratory deterioration in select patients with COVID-19, who require oxygen supplementation or NIV/CPAP. This in turn may reduce demand for IMV, easing the strain placed on intensive care services around the world. In resource-limited settings, this simple, low-cost intervention may serve to raise the ceiling of care for patients that might otherwise have no further option. However, a blanket policy for awake prone positioning in COVID-19, as advocated by ICS, may overstretch personnel without achieving clinically tangible benefits. This may be particularly relevant outside of critical care settings, where staff is likely to be inexperienced and untrained in the adoption of prone positioning.

Presently, uncertainties surrounding the effectiveness of awake prone positioning in ARDS and COVID-19 are substantial. High-quality studies are required to assess the degree to which awake prone positioning may be beneficial, as well as select those who may benefit from it the most. With such an easy intervention, there may be a temptation to intervene based on compassionate grounds—however, without evidence, it will be difficult to assess the true value of prone positioning for future pandemics.

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