



Management of respiratory failure due to covid-19

Pathology and management are similar to acute respiratory distress syndrome

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The most concerning complication of SARS-CoV-2 infection (covid-19) is acute hypoxaemic respiratory failure requiring mechanical ventilation. Numerous mechanisms have been suggested for the substantial hypoxaemia seen in many patients.¹ These include pulmonary oedema, haemoglobinopathies, vascular occlusion, and a mismatch between ventilation and perfusion.

The available histopathology, however, shows diffuse alveolar damage² consistent with acute respiratory distress syndrome (ARDS). Several of the other suggested aetiologies are also consistent with ARDS, and microvascular and macrovascular thrombi in ARDS have been recognised for decades.³ The variable pulmonary compliance associated with severe covid-19 is comparable with pulmonary compliance values reported for ARDS.^{4,5} The heterogeneity of ARDS is well documented, with distinct subtypes related to the degree of inflammation and response to positive end expiratory pressure (PEEP).^{5,6} Overall, the pathology seen in patients with covid-19 is very similar to established descriptions of ARDS.

Oxygen therapy

The trivial dyspnoea experienced by some patients with demonstrable hypoxaemia has led to debates about the need for oxygen therapy. However, hypoxaemia is a poor stimulus for dyspnoea, and variation in symptoms associated with hypoxaemia is unsurprising. Even for patients with minimal symptoms, available evidence does not support tolerating hypoxaemia. A recent randomised trial comparing liberal (target oxygen saturation $\geq 96\%$) and conservative (target 88-92%) strategies for oxygen therapy in patients with ARDS was stopped early after it became clear that the conservative approach was unlikely to benefit patients and might cause harm.⁷ Recent guidance recommends a target oxygen saturation of 92-96% in adults with covid-19, using supplemental oxygen as needed.⁸

Some patients will require support beyond supplemental oxygen, and the choice between high flow nasal cannula, non-invasive positive pressure ventilation, or early intubation has been controversial. Issues include the need to protect healthcare workers from exposure to viral aerosols while providing optimal care for patients.

Oxygen delivered through high flow nasal cannulas is beneficial in hypoxaemic respiratory failure⁹ and can provide up to 60 L/min of nearly 100% oxygen. The risk of virus aerosols from this delivery method is probably low,¹⁰ although concerns remain. Patient selection is critical; those with moderate to severe hypoxaemia are unlikely to get enough oxygen through high flow nasal cannulas and will usually require intubation.¹¹ Stable patients with isolated mild to moderate hypoxaemia can be given oxygen through nasal cannulas but should be monitored carefully for signs of deterioration.

Non-invasive ventilation

Non-invasive positive pressure ventilation (NIPPV) provides ventilatory support without the need for an endotracheal airway, so patients remain awake. While this option is non-invasive it isn't completely benign. Patients retain some control over their breathing and large volume breaths can cause self-inflicted lung injury,¹² which has been associated with higher mortality among patients subsequently admitted to an intensive care unit with ARDS.¹³ In one small retrospective case series from Wuhan, 72% of covid-19 patients given NIPPV died, although death rates were also high for patients intubated from the outset.¹⁴

NIPPV is associated with a variable and hard to quantify risk of aerosol generation, which may depend on the tightness of the seal around a patient's mask.¹⁵ Given the unclear benefit to patients, non-invasive ventilation is probably of limited value in patients with hypoxaemic respiratory failure due to covid-19.¹⁵

Uncertainty about how best to optimise respiratory support has led to increased use of prone positioning for patients who are not intubated (awake proning). Lying prone improves ventilation-perfusion matching and is associated with reduced mortality among patients with ARDS, when compared with supine positioning.⁴ Observational evidence from patients with viral ARDS and with covid-19^{16,17} provides reasonable support for a trial of awake proning in selected patients, particularly as it is a low risk intervention.

Intubation

Arguments for and against early intubation are not yet resolved, largely because good evidence is lacking. Those who

recommend prompt intubation suggest that it avoids the risk of self-induced lung injury.¹⁸ Those who argue against early intubation note the high death rates reported among intubated patients with covid-19 and cite concerns that ventilator induced lung injury is a contributing factor. The best approach will likely vary by patient. A single approach is unlikely to work in a disease as heterogeneous as covid-19.

Since ARDS caused by covid-19 is similar to ARDS with other causes, the principles underpinning ventilation should also be similar: provide ventilation to protect the lungs with low tidal volumes, low driving pressures, and titration of positive end expiratory pressure to meet each patient's needs, with the overall goal of improving lung compliance.

Substantial evidence shows that protective ventilation with lower tidal volumes and pressures is strongly associated with improved outcomes in patients with ARDS.¹⁹ Patients who remain hypoxaemic despite optimal ventilation should be considered for prone positioning while intubated.⁴

Data may be scarce, but we have enough to support evidence based management of covid-19— from optimising oxygenation, providing respiratory support, intubating when necessary, and tailoring ventilatory pressure to patients' specific needs.

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