In brief

Respiratory therapies and COVID-19

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Summary

- Clinical management of COVID-19 includes monoclonal antibodies, antiviral drugs and supportive therapies. Respiratory therapies may be used to manage acute respiratory failure, providing ventilatory support and reducing the need for intubation and admission to intensive care.[1] They include oxygen delivery devices, non-invasive ventilation, high flow nasal oxygen therapy and prone positioning.
- Respiratory supports may be used to provide oxygen for adults with COVID-19. Alternatives to invasive mechanical ventilation include standard oxygen delivery devices; non-invasive ventilation, including continuous positive airway pressure (CPAP); and high flow nasal oxygen therapy.
    - Standard oxygen delivery devices, including nasal cannulas, simple (Hudson) masks, Venturi masks and non-rebreather masks deliver varying levels of oxygen to COVID-19 patients with hypoxaemia.
    - The Australian National COVID-19 Clinical Evidence Taskforce recommends non-invasive ventilation for patients with hypoxaemia.[3] Non-invasive ventilation may reduce mortality and the need for invasive mechanical ventilation.[2, 3]
    - The Taskforce recommends CPAP in COVID-19 patients with severe hypoxaemia who are not suitable for mechanical ventilation.[4, 5] CPAP has been found to have a positive effect on oxygenation and respiratory rate[6] and early use may reduce mortality.[7]
    - The Taskforce recommends high flow nasal oxygen therapy when a patient is unable to maintain oxygen saturation above 92%.[3] The National Institute of Health COVID-19 treatment guideline recommends high flow nasal cannula over non-invasive positive pressure ventilation.[8]
- Prone positioning has been shown to significantly decrease 28-day and 90-day mortality in critically-ill patients with non-COVID-19 acute respiratory distress syndrome (ARDS).[9] The Australian National COVID-19 Clinical Evidence Taskforce and the World Health Organization (WHO) recommend prone positioning.[2, 10]
- Many respiratory therapies are considered to be aerosol-generating procedures (AGPs). The WHO considers intubation, extubation, non-invasive ventilation, CPAP, BiPAP, and high-flow oxygen therapy to be AGPs.[11]

Respiratory supports in adults with COVID-19

Standard oxygen delivery devices

- Standard oxygen delivery devices include:
    - Nasal cannula: can be used at 1-6 L/minute as an initial strategy for COVID-19 patients with mild hypoxaemia.[12, 13]
    - Simple (Hudson) mask: can be used to deliver an oxygen flow of 5-10 L/minute. For patients requiring higher oxygen delivery, a non-rebreather mask should be used.[12, 14]
    - Venturi mask: allows for more precise oxygen titration of up to 50% and should be covered with a surgical mask. Alternatively, a non-rebreather mask can be used.[15]

- Non-rebreather mask: delivers oxygen flow at 10-15 L/minute and is preferred over a simple mask as it generates the least aerosol dispersion distances (<10cm) compared to other oxygen modalities.[16, 17] It should be covered with a surgical mask [14-16, 18, 19] and, if possible, with a filtered exhalation port.[20]

Non-invasive ventilation

- Non-invasive ventilation (NIV), also known as non-invasive positive pressure ventilation (NIPPV) or bilevel positive pressure support (BiPAP), is a form of respiratory support in which bilevel positive pressure is delivered by a firm-fitting nasal-face mask. Supplemental oxygen can also be delivered through the device.[2]
- The Australian National COVID-19 Clinical Evidence Taskforce guidelines conditionally recommend non-invasive ventilation for COVID-19 patients with hypoxaemia, ideally in a negative pressure room.[2]
- A living systematic review reported that non-invasive ventilation probably reduces mortality and the need for invasive mechanical ventilation, but may increase the risk of COVID-19 transmission to healthcare workers.[3]
- A systematic review of guidelines for non-invasive ventilation during COVID-19 suggested use in a single room, negative-pressure ward, or a dedicated COVID-19 ward. Healthcare workers should wear full personal protective equipment including eye protection, N95 or higher respirators, gloves, and long-sleeved gowns.[21]
- Non-invasive ventilation should not be used in place of invasive ventilation or endotracheal intubation in patients with deteriorating respiratory status, hemodynamic instability, multiorgan failure, or abnormal mental status.[21]
- A case report on the use of average volume-assured pressure support (AVAPS) in a COVID-19 patient unable to tolerate extubation to high flow nasal cannula found AVAPS successfully supported ventilation and oxygenation non-invasively.[22]

Continuous positive airway pressure

- CPAP is a non-invasive form of positive airway pressure ventilation that delivers a constant pressure through the respiratory cycle. CPAP is recommended in COVID-19 patients with severe hypoxaemia who are not suitable for mechanical ventilation.[4, 5]
- The Australian National COVID-19 Clinical Evidence Taskforce conditionally recommends CPAP for COVID-19 patients with persistent hypoxaemia. Most patients require pressures of 10 to 12 cm and oxygen should be adjusted to maintain SpO_2 in the target range (FiO_2 0.4-0.6).[2]
- Guidelines from the UK National Health Service (NHS) suggest that if the patient is oriented and able to tolerate a well-fitted, non-vented face mask, CPAP should be set to 10cm$H_2$0, with FiO_2 0.6, and increased to 12–15cmH_2O, with FiO_2 0.6–1.0 if needed. Other guidelines suggest setting the CPAP value at 10–12cmH_2O and increasing up to 15–20cmH_2O if escalation is needed.[21]
- In an observational study of COVID-19 patients treated with CPAP, CPAP was initiated when oxygen supplementation exceeded 10 litres/minute to maintain oxygen saturation (SpO_2) ≥92%. CPAP was administered with full face masks on a continuous basis until stable improvement in oxygenation or until intubation or death. CPAP had a positive effect on oxygenation and respiratory rate in most patients but the prognosis for elderly patients with high oxygen requirements was poor.[6]
- A pre-print randomised controlled trial found CPAP reduced intubation or death within 30 days compared to conventional oxygen therapy in hospitalised adults with COVID-19.[23] Conversely, an observational study comparing clinical outcomes in COVID-19 patients not suitable for invasive mechanical ventilation found no differences between oxygen therapy alone compared to CPAP.[24]

- The timing of treatment may be important, with early use (within four days of hospital admission) of CPAP linked to a reduction in mortality.[7]

High flow nasal oxygen therapy

- High flow nasal oxygen therapy is a form of non-invasive ventilation where oxygen is delivered via nasal cannula, often in conjunction with compressed air and humidification. Flow rates can be given up to 60 L/minute with an oxygen/air blender supplying oxygen at 21-100%.[2]
- The Australian National COVID-19 Clinical Evidence Taskforce guidelines conditionally recommend high flow nasal oxygen therapy as an alternative, if CPAP is not available or tolerated.[2]
- The National Institute of Health COVID-19 treatment guideline recommends high flow nasal cannula over non-invasive positive pressure ventilation for adults with COVID-19 and acute hypoxemic respiratory failure, despite conventional oxygen therapy. This recommendation is based on clinical trials comparing the outcomes of these two methods.[8]
- High flow oxygen therapy may cause aerosolisation of viral pathogens.[14, 15, 18, 25-28] However, there is no clear evidence as to whether high flow nasal cannula has lower risk of nosocomial transmission than non-invasive ventilation, or vice versa.[8]
- Recommendations for caring for suspected or confirmed COVID-19 patients include:
  - use the lowest flow necessary[2]
  - ensure correct placement of the nasal cannula and attach elastic bands to the patient's head securely[17]
  - use a surgical mask over the high-flow nasal cannula to reduce viral transmission[14, 17]
  - maintain a closed-circuit, do not interrupt oxygen supply arbitrarily during high flow oxygen therapy[17, 18, 26, 29, 30]
  - stay more than 45 centimetres away from the patient's airway, and if clinically appropriate, maintain a physical distance of one metre or more from the patient[18]
  - use high-flow nasal cannula in a well-ventilated area[30, 31]
  - treat in a negative-pressure room, or if unavailable,[14] a single room with door closed[2, 28] or shared ward spaces with a cohort of suspected or confirmed COVID-19 patients.[2]
  - minimise patient transfer.[2]

Principles of weaning respiratory supports

- The ability to successfully wean a COVID-19 patient off ventilation is related to patient outcomes, including mortality rate.[32]
- An observational study reported COVID-19 patients with severe acute respiratory distress syndrome (ARDS) required twice as long (11 days) to wean off invasive mechanical ventilation compared to non-severe ARDS (5 days).[33]
- In a study of 18 ventilated COVID-19 patients in Israel, 88% were successfully weaned from mechanical ventilation and decannulated in a median time of 10 days.[34]
- A review on weaning precautions in critically-ill COVID-19 patients suggested patients should have a patent airway, adequate ventilation and gas exchange capacity with minimal or no respiratory stress before extubation. Methods of weaning in COVID-19 patients include progressive reduction of pressure support and daily breathing trials.[35]
- In two case reports on critical COVID-19 patients, weaning was successfully achieved using a weaning screening test, spontaneous breathing test and an airbag leak test. Patients were transitioned to non-invasive ventilation and high flow nasal cannula oxygen support.[36]
- An observational study on weaning COVID-19 patients from helmet CPAP included a weaning trial of reduction in support to minimal positive end-expiratory pressure (PEEP≈2 cmH2O, including

antiviral filters) maintaining a FiO2 ≤ 60%. Absence of respiratory distress and SpO2 ≥ 94% in the subsequent 30 minutes lead to helmet removal and oxygen supplementation with FiO2 ≤ 60%.[37]

Prone positioning

- Prone positioning is a technique used to help patients with acute respiratory distress syndrome (ARDS) breathe better by placing them on their stomach. Prone positioning is generally used for sedated patients requiring a ventilator but may be beneficial in awake patients with COVID-19.[38]
- Evidence from randomised controlled trials of prone positioning for intubated, critically-ill patients with non-COVID-19 ARDS have demonstrated that prolonged prone positioning sessions significantly decreased 28-day and 90-day mortality.[9]
- The Australian National COVID-19 Clinical Evidence Taskforce guidelines recommend prone positioning for more than 12 hours per day in mechanically ventilated adults with COVID-19 and hypoxaemia. Prone positioning for at least three hours per day is conditionally recommended for adults with COVID-19 and respiratory symptoms receiving any form of supplemental oxygen therapy and who have not been intubated.[2]
- The WHO guidelines recommend prone ventilation for 12–16 hours per day for adult patients with severe acute respiratory infection with COVID-19.[10]
- Two systematic reviews on the effectiveness of prone positioning in patients with COVID-19 reported potential benefits associated with improved oxygenation parameters and reduced mortality.[39, 40] One reported a decreased intubation rate,[39] while the other found no significant effect on incidence of intubation or critical care admission.[40] Prone positioning had no significant effect on respiratory rate.[39]
- Two observational studies of patients with COVID-19 found alternating supine and prone positioning was associated with increased lung recruitability,[41] and prone positioning provides better ventilation of the dorsal lung regions.[42]
- Awake prone positioning may cause patient discomfort and pain.[43] Complications can occur during transitions to and from prone positioning, including:
    - device displacement
    - vomiting
    - loss of venous access
    - accidental extubation
    - endotracheal tube displacement and obstruction
    - hemodynamic instability
    - brachial plexus injury and pressure ulcers.[44]
- Some studies have reported the development of pressure injuries (skin and underlying tissue) in patients with ARDS who were placed in a prone position.[45, 46] One study demonstrated that having a certified wound and skin care nurse lead pressure injury prevention on a prone positioning team was significantly associated with lower odds of pressure injuries developing in COVID-19 patients.[47]

Aerosol generating procedures

- Aerosol-generating procedures (AGPs) increase transmission risk for respiratory pathogens because they produce aerosols.[48] Airborne transmission of COVID-19 may occur during aerosol-generating procedures.[49]
- The World Health Organization lists the following as AGPs associated with an increased risk of COVID-19 transmission:
    - tracheal intubation
    - non-invasive ventilation (e.g. BiPAP, CPAP)

    - tracheotomy
    - cardiopulmonary resuscitation
    - manual ventilation before intubation
    - bronchoscopy
    - sputum induction induced by using nebulised hypertonic saline
    - autopsy procedures.

  The association between nebuliser therapy or high-flow oxygen and COVID-19 transmission is unclear as data is limited.[11]
- The US Centers for Disease Control and Prevention guidance considers the following procedures AGPs:
    - open suctioning of airway secretions
    - sputum induction
    - cardiopulmonary resuscitation
    - endotracheal intubation and extubation
    - non-invasive positive pressure ventilation (e.g. BiPAP, CPAP)
    - bronchoscopy
    - manual ventilation
    - autopsy procedures
    - medical/surgical procedures.[50]
- The Clinical Excellence Commission classifies high-flow nasal cannula and non-invasive ventilation as high risk AGPs.[28]
- A rapid systematic review classified 39 procedure groups associated with aerosol generation:
    - intubation and extubation
    - bronchoscopy
    - sputum induction
    - manual ventilation
    - airway suctioning
    - cardiopulmonary resuscitation
    - tracheostomy and tracheostomy procedures
    - non-invasive ventilation
    - high-flow oxygen therapy
    - nebulised or aerosol therapy.[51]
- A separate systematic review found endotracheal intubation, non-invasive ventilation, and administration of nebulised medications, increased the odds of healthcare workers being infected with COVID-19.[52]
- A pre-print study comparing emissions from ten healthy subjects during respiratory 'activities' (quiet breathing, talking, shouting, forced expiratory manoeuvres, exercise, and coughing) with respiratory therapies found that talking, exertional breathing and coughing generate substantially more aerosols than respiratory therapies.[53]

To inform this brief, a series of Critical Intelligence Unit evidence briefs were used as the base information for the document. Supplementary PubMed and Google searches were conducted using terms related to respiratory therapies, oxygen therapy, aerosol-generating procedures, prone positioning, non-invasive ventilation, continuous positive airway pressure, weaning, and COVID-19 on 11 and 12 October 2021.

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