Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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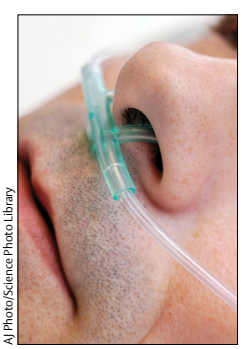
COVID-19: Respiratory support outside the intensive care unit



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For **NHS guidelines** see https://www.england.nhs.uk/coronavirus/secondary-care/other-resources/specialty-guides/#adult-critical-care

For **Irish Thoracic Society guidelines** see https://irishthoracicsociety.com/2020/03/irish-thoracic-society-covid-19-guidelines-for-managing-respiratory-care/

For **ARDSnet guidelines** see https://www.thoracic.org/statements/resources/cc/ards-guidelines.pdf

The optimal mode of respiratory support for individuals with severe coronavirus disease 2019 (COVID-19) before invasive mechanical ventilation (IMV) is currently a subject of much debate. Recently published guidelines[1] and a Comment[2] differ substantially to other guidelines in this regard, with some advocating high flow nasal cannulae (HFNC) over non-invasive ventilation (NIV),[1,2] or vice versa (NHS guidance). This debate is understandable given the paucity of data and need for rapid generation of guidance, but it is a cause of confusion among respiratory physicians.

Much of the data guiding practice in this area derive from the critical care setting. In acute respiratory distress syndrome (ARDS), early intubation was associated with survival benefit when PaO_2/FiO_2 ratio was <150 when compared with NIV.[3] Some COVID-19 guidelines have therefore suggested NIV as a bridging therapy only, before transfer to the intensive care unit (ICU) and IMV. However, up to 50% of patients with COVID-19 admitted to the ICU did not subsequently require IMV.[4] Given the considerable resource limitations imposed by the current unprecedented viral pandemic, it is important to ascertain whether selected patients can be safely managed outside of the ICU.

To our knowledge, there have been no randomised control trials in the use of either HFNC or NIV in coronavirus-related pneumonia. It has been reported that use of NIV during the Middle Eastern respiratory syndrome outbreak was associated with a 92% risk of requiring IMV, thus suggesting futility.[5] This study was based in the ICU, however, and patients enrolled had a median PaO_2/FiO_2 ratio of 110 (IQR 62–160), indicating a degree of severity that likely warranted initial management with IMV. Conversely, data from only one study[6] on the severe acute respiratory syndrome (SARS) outbreak suggest that NIV can successfully avoid intubation.

HFNC has received much interest since the FLORALI trial.[7] Acute hypoxaemic respiratory failure (AHRF) in this study was largely secondary to community or hospital-acquired pneumonia. Though the primary outcome of intubation at day 28 was negative, HFNC reduced requirement for intubation in a subgroup of patients with PaO_2/FiO_2 ratio <200 and was associated with a reduction in mortality when compared with NIV or regular oxygen face mask. The NIV group of this study involved NIV use for an average of only 8 h per day, however, and a relatively high target tidal volume of 7–10 mL/kg. FLORALI also utilised a flow rate of 50 L/min with HFNC. To ameliorate potential aerosol generation, a flow limit of 30 L/min in COVID-19 has been proposed. The level of positive end-expiratory pressure (PEEP) supplied is consequently reduced. Notably, with regards to aerosol generation and risk to health-care workers, intubation poses a greater risk than NIV and a risk with HFNC has not been established.[8]

Concern regarding ward oxygen flow rates and hospital oxygen reserves is probably the most important cause for hesitancy over advocating HFNC (Irish Thoracic Society Guidelines). A major benefit of PEEP is that it might allow for down-titration of FiO_2, mitigating against over-consumption of hospital oxygen supply and avoiding hyperoxia-related lung injury. Anecdotal reports and our own experience of COVID-19-related lung injury suggests a good response to application of PEEP, perhaps related

to recruitment of atelectasis and reduced work of breathing. PEEP of 10 cm H_2O or higher can shift the lung to the point on the pressure–volume curve with the highest slope (high compliance).[9] Haemodynamic instability appears to be a relatively infrequent feature of these patients, and thus higher PEEP (ie, expiratory positive airway pressure) than traditionally applied with NIV is likely to be tolerated well.

Benefits of bi-level positive airway pressure over continuous positive airway pressure in this setting have not been established conclusively. Regardless of mode, the key factor in improving oxygenation is mean airway pressure (Paw). Addition of pressure support has the advantage of compensating for resistance present in the tubing and in further reducing work of breathing.[10] It is prudent to follow ARDSnet guidelines in maintaining tidal volume of ≤6 mL/kg through low pressure support (driving pressure), relatively high PEEP, and the lowest FiO_2 feasible. To mitigate against nosocomial aerosol transmission, it is critical that NIV circuits are modified to include a filter at the exhalation port or vent.

The debate about the optimal mode of respiratory support before IMV in AHRF has not been settled, much less in the setting of coronavirus, and it is important to note that harm can be caused if inappropriate treatment is used.[3] Evidence from China[11] suggests that a large minority of patients with severe respiratory failure due to SARS coronavirus 2 (SARS-CoV-2) can avoid intubation via use of NIV however. NIV is a well-established therapy with which general respiratory physicians and nurses are familiar, and which is readily applicable in the non-critical care setting. Caveats would include careful patient selection so as not to delay IMV where appropriate, modified settings specific to the pathophysiology of COVID-19, and mitigation against infection transmission by aerosol.

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Hydroxychloroquine in the management of critically ill patients with COVID-19: the need for an evidence base

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With the rapid spread of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), critical care physicians are seeing increasing numbers of patients with acute respiratory failure secondary to coronavirus disease 2019 (COVID-19) and reporting mortality rates of 40–65% for those requiring mechanical ventilation[1]—strikingly higher than the mortality rates reported for the more typical acute respiratory distress syndrome associated with other diseases.[2] The focus of therapeutic intervention has therefore been not only to reverse hypoxaemia and provide adequate organ support, but also to decrease viral load and thus limit disease severity. In addition to several antiviral agents, antimalarial drugs have been proposed as treatments that could reduce transmission of the virus. In-vitro studies have shown that chloroquine and hydroxychloroquine can both inhibit SARS-CoV-2 transmission,[3-5] through