The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our National Health Library and Knowledge Service Summary of Evidence Protocol.

YOUR QUESTION

What is the evidence to support prone positioning of awake COVID-19 patients receiving non-invasive ventilation or ventilating on room air?

IN A NUTSHELL

The prone position consists of placing the patient on his or her stomach with the head on the side during sessions lasting several hours a day with the aim of assisting in the spontaneous ventilation[7].

Based on improvements observed with mechanically ventilated patients, it has been postulated that adopting the prone position for conscious COVID-19 patients requiring basic respiratory support may also improve oxygenation, reduce the need for invasive ventilation and potentially reduce mortality[3]. Guérin et al.[14] state that in patients with severe acute respiratory distress syndrome (ARDS), early application of prolonged prone positioning sessions significantly decreased 28-day and 90-day mortality.

Sun et al[10] report on a study from China that outlines how adopting the awake prone position in novel coronavirus pneumonia patients showed significant effects in improving oxygenation and pulmonary heterogeneity. Ding et al[12] conclude that early application of prone positioning with high-flow nasal cannula, especially in patients with moderate ARDS and baseline SpO2 > 95%, may help avoid intubation. Prone positioning was well tolerated, and the efficacy on PaO2/FiO2 of the four support strategies was HFNC < HFNC+PP ≤ NIV < NIV+PP. Severe ARDS patients were not appropriate candidates for HFNC/NIV+PP.

Some experts are suggesting that the hospitalized patient spend as much time as is feasible and safe in the prone position while receiving oxygen; their rationale is based on limited direct evidence and anecdotal observations in the field as well as indirect evidence of the efficacy of prone positioning in ventilated patients[6].

IRISH AND INTERNATIONAL GUIDANCE

Intensive Society of Ireland (2020). Guidance document for the Intensive Care Management of the adult patient with confirmed or suspected COVID-19[1]

Management of Hypoxic Respiratory Failure and MOF NIV

"Yes, we are using NIV, we are using everything"
Maurizio Cecconi MD, March 13, 2020, Lombardy

NIV will almost certainly be an inevitable intervention if we are faced with a significant expansion in ICM facilities; it would be naïve to think otherwise. The most salient message from the Chinese and Italian experience, where NIV is being extensively used, is early switch to IPPV if the patient does not stabilise on NIV.
The ICSI also acknowledges that patients under the care of respiratory physicians may well be receiving NIV on the wards outside of the sphere of ICU. Therefore, we should have guidance about the safest utilisation of NIV rather than guidance merely to avoid NIV. Clear lines of communication between respiratory medicine and ICU is vital.
Points to note:

- NIV is an aerosol generating procedure and should not be used in open spaces in ICU, ED or wards in COVID-19 positive or suspect cases.
- Thus, NIV should be used in single isolation rooms with full PPE.
- NIV has been used successfully in less severe disease and post-extubation and can be maintained on patients as long as there is no fatigue.
- Clinical fatigue warrants immediate consideration of IPPV if appropriate. Fatigue with progression to IPPV tends to occur early in COVID-19 patients.
- Correctly fitting facemasks are key to NIV efficiency and reduction in aerosolization.
- Data surrounding HFNO as an AGP is less robust but international consensus leans towards considering it as such and thus is grouped with NIV.

— In advanced situations where isolation resources are exhausted consider cohorting such NIV dependent COVID-19 patients into designated rooms/wards with full PPE available for staff.

Summary: the main side-effects of NIV are not knowing its limitations in the COVID-19 patient.

What does the World Health Organization say?

World Health Organization (2020). Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance 13 March 2020[2]

In adult patients with severe ARDS prone ventilation for 12–16 hours per day is recommended.
re Paediatric Patients: Application of prone ventilation is strongly recommended for adult patients, and may be considered for paediatric patients with severe ARDS but requires sufficient human resources and expertise to be performed safely. Protocols including videos are available.
re Pregnant Women: There is little evidence on prone positioning in pregnant women. Pregnant women may benefit from being placed in lateral decubitus position.

Intensive Care Society (UK) (2019). Guidance for Prone Positioning in Adult Critical Care[3]

Over the last two decades randomised controlled trials have consistently demonstrated that oxygenation can be significantly improved in patients with acute respiratory distress syndrome (ARDS) when ventilated in the prone position. Early trials of prone ventilation failed to demonstrate any impact on mortality, although these trials were conducted in an era prior to lung protective ventilation, often had patients proned for short periods and included patients with mild ARDS. As trial design evolved to include modern ventilation practices along with patients with more severe ARDS, evidence emerged that the early application of prolonged prone positioning may significantly decrease mortality compared to conventional supine ventilation. This stance has been further supported by a recent meta-analysis that concludes mechanical ventilation in the prone position significantly reduces mortality in patients with moderate to severe ARDS when used early and for greater than 16 hours per day in patients receiving lung protective ventilation. In addition, a Cochrane systematic review published in 2015 recommends that prone ventilation for 16 or more hours

per day should be actively considered in patients with severe hypoxaemia within 48 hours of mechanical ventilation. This has also led to the inclusion of prone ventilation in the ARDS guidance published by the Intensive Care Society and Faculty of Intensive Care Medicine. These recommendations would suggest the use of early prone ventilation for moderate to severe hypoxaemia and potentially an increase in the number of patients that should be considered for proning. The increase in use of the prone position in critical care may have been partially responsible for a spike in critical incidents reported to NHSi over recent years. At the end of 2017, NHSi approached the ICS/FICM Joint Standards Committee with the hope that the committee might identify a strategy to reduce the number of incidents moving forward. With this in mind the ICS/FICM JSC performed a national survey of its members to identify current practices across the UK and to identify whether there was a need for a national guidance on managing patients in the prone position.

NHS England (2020). Guidance for the role and use of non-invasive respiratory support in adult patients with COVID19 (confirmed or suspected)[4]

This guidance should be used to advise clinicians on the appropriate use of continuous positive airway pressure [CPAP], non-invasive ventilation [NIV, here referring to bilevel positive airway pressure, BIPAP] and high flow nasal oxygen [HFNO, such as OptiflowTM] in patients with confirmed or suspected COVID-19. Published evidence, clinical guidelines and personal communications with colleagues in China and Italy have informed this document.

POINT-OF-CARE TOOLS

What does BMJ Best Practice say?

Coronavirus Disease 2019 (COVID-19)[5]

Section: Treatment Algorithm

Consider prone ventilation for 12 to 16 hours per day in patients with persistent severe hypoxic failure. Pregnant women may benefit from being placed in the lateral decubitus position. A small cohort study of 12 patients in Wuhan, China, with COVID-19-related acute respiratory distress syndrome suggests that spending periods of time in the prone position may improve lung recruitability.

What does UpToDate say?

Respiratory Care of the Non-Intubated Patient[6]

Specific aspects of respiratory care relevant to deteriorating patients with COVID-19 before admission to the intensive care unit are discussed here. These include oxygenation with low flow and high-flow systems, non-invasive ventilation and the administration of nebulized medications. For hospitalized patients who develop progressive symptoms, early admission to the ICU is prudent when feasible. Some experts are encouraging that the hospitalized patient spend as much time as is feasible and safe in the prone position while receiving oxygen; the rationale for this approach is based upon limited direct evidence and anecdotal observations in the field as well as indirect evidence of its efficacy in ventilated patients.

INTERNATIONAL LITERATURE

What does the international literature say?

Bamford et al. (2020) ICS Guidance for Prone Positioning of the Conscious COVID Patient 2020[7]

The recent COVID-19 pandemic has seen the critical care community treating increasing numbers of patients with ARDS over recent weeks, with one Chinese study reporting the prevalence of hypoxic respiratory failure in these patients at around 19%. Approximately 5% of all COVID-19 patients will

require mechanical ventilation on an intensive care unit, with a further 14% requiring oxygen therapy.
Internationally, observations of critical care clinicians have reported that patients with moderate to severe ARDS appear to have responded well to invasive ventilation in the prone position, leading to prone ventilation being recommended in international guidelines for the management of COVID-19. This corroborates well with the findings of the PROSEVA trial, a recent meta-analysis and a Cochrane systematic review, all of which support the early use of prone ventilation in patients with moderate to severe ARDS to improve oxygenation and reduce mortality when compared with conventional supine ventilation.
Given the improvement in mechanically ventilated patients, it has been postulated that adopting the prone position for conscious COVID-19 patients requiring basic respiratory support may also benefit patients in terms of improving oxygenation, reducing the need for invasive ventilation and potentially even reducing mortality.

ProCOV (2020) [CLINICAL TRIAL. Prone Positioning in Spontaneously Breathing Nonintubated COVID-19 Patient: a Pilot Study (ProCov)[8]

SARS-CoV-2 is an RNA virus whose tropism for the respiratory system is responsible for many cases of acute respiratory failure. This can lead to acute respiratory distress syndrome (ARDS) requiring orotracheal intubation and mechanical ventilation. The prone position is a validated intensive care technique in the treatment of ARDS in mechanically ventilated patients. Performing prone position sessions improves patient oxygenation by optimizing the ventilation/perfusion ratios of the posterior areas of the lungs. There is limited data in the literature on the ventral decubitus in spontaneous ventilation. They are mainly case series or retrospective studies. In the case of the SARS-CoV-2 epidemic, we are seeing patients with posterior lung involvement who may benefit from prone position sessions prior to mechanical ventilation. This maneuver, usually done in an intubated-ventilated-curarized patient, will be done in our spontaneous ventilation study in a conscious patient. The patient will then be placed in prone position with the help of physiotherapists so that the patient is correctly positioned. The maneuver and the clinical monitoring of the patient's tolerance to the prone position will be done under medical and paramedical supervision, including monitoring of saturation during and after the procedure. A polygraph will also be installed on the patient in order to monitor the patient's position — on the back vs. on the stomach — saturation and heart

rate during the entire prone position session. An arterial gasometry will be performed before the patient is placed in the prone position, one hour after and after returning to the supine position.

Gordon (2020) COVID-19: Awake Pronation[9]

Awake proning has been widely popularized in the era of COVID-19. Outside of COVID-19 several case studies have reported success with proning in awake patients. These case reports are heterogenous and include reports of patients with a variety of underlying etiologies of respiratory disorders and various approaches to respiratory support. Nonetheless, all cases describe generally short periods of intermittent proning that is well tolerated with either laboratory, radiographic or clinical improvement.

Sun et al (2020) Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province[10]

Although previous study proved prone position's benefit in moderate-to-severe ARDS patients with invasive mechanical ventilation, we attempted awake prone position in NCP patients which showed significant effects in improving oxygenation and pulmonary heterogeneity. With all these measurements, although the rate of critically ill patients in Jiangsu had reached 10%, the IMV rate of Jiangsu was kept under 1%, which was significantly lower than our previous survey about ARDS patients.
[See especially: Figure 2.]

Duca et al (2020) Calculated Decisions: Brescia-COVID Respiratory Severity Scale (BCRSS)/Algorithm[11]

The Brescia-COVID respiratory severity scale/algorithm is a stepwise management approach to COVID-19 patients based on clinical severity. The BCRSS was rapidly developed in Brescia, Italy, during that nation's COVID-19 crisis. The scale has not been validated or tested in other populations. The BCRSS uses patient examination features along with the need for escalating levels of respiratory support—NIV, intubation, proning—to suggest treatment recommendations. The scale simplifies the clinical summary of a patient's status, and allows clinicians to compare patients to one another and to track the trend of a patient's level of respiratory severity over time.

Ding et al (2020) Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study[12]

Previous studies suggest that prone positioning can increase PaO2/FiO2 and reduce mortality in moderate to severe ARDS. The aim of our study was to determine whether the early use of PP combined with non-invasive ventilation or high-flow nasal cannula can avoid the need for intubation in moderate to severe ARDS patients.

This prospective observational cohort study was performed in two teaching hospitals. Non-intubated moderate to severe ARDS patients were included and were placed in PP with NIV or with HFNC. The efficacy in improving oxygenation with four support methods—HFNC, HFNC+PP, NIV, NIV+PP—were evaluated by blood gas analysis. The primary outcome was the rate of intubation.

Between January 2018 and April 2019, 20 ARDS patients were enrolled. The main causes of ARDS were pneumonia due to influenza (9 cases, 45%) and other viruses (2 cases, 10%). Ten cases were moderate ARDS and 10 cases were severe. Eleven patients avoided intubation [success group], and 9 patients were intubated [failure group]. All 7 patients with a PaO2/FiO2 < 100 mmHg on NIV required intubation. PaO2/FiO2 in HFNC+PP were significantly higher in the success group than in the failure group: 125 ± 41 mmHg vs 119 ± 19 mmHg, P = 0.043. PaO2/FiO2 demonstrated an upward trend in patients with all four support strategies: HFNC < HFNC+PP ≤ NIV < NIV+PP. The average duration for PP was 2 h twice daily.

Conclusions

Early application of PP with HFNC, especially in patients with moderate ARDS and baseline SpO2 > 95%, may help avoid intubation. The PP was well tolerated, and the efficacy on PaO2/FiO2 of the four support strategies was HFNC < HFNC+PP ≤ NIV < NIV+PP. Severe ARDS patients were not appropriate candidates for HFNC/NIV+PP.

Scaravilli (2015) Prone positioning improves oxygenation in spontaneously breathing non-intubated patients with hypoxemic acute respiratory failure: A retrospective study[13]

Prone positioning improves oxygenation and outcome of patients with acute respiratory distress syndrome undergoing invasive ventilation. Scaravilli evaluated the feasibility and efficacy of PP in awake, non-intubated, spontaneously breathing patients with hypoxemic acute respiratory failure and concluded that PP was feasible and improved oxygenation.

Guerin et al (2013) Prone positioning in severe acute respiratory distress syndrome[14]

Previous trials involving patients with the acute respiratory distress syndrome have failed to show a beneficial effect of prone positioning during mechanical ventilatory support on outcomes. We evaluated the effect of early application of prone positioning on outcomes in patients with severe ARDS.

In this multicenter, prospective, randomized, controlled trial, we randomly assigned 466 patients with severe ARDS to undergo prone-positioning sessions of at least 16 hours or to be left in the supine position. Severe ARDS was defined as a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (FiO2) of less than 150 mm Hg, with an FiO2 of at least 0.6, a positive end-expiratory pressure of at least 5 cm of water, and a tidal volume close to 6 ml per kilogram of predicted body weight. The primary outcome was the proportion of patients who died from any cause within 28 days after inclusion.

A total of 237 patients were assigned to the prone group, and 229 patients were assigned to the supine group. The 28-day mortality was 16.0% in the prone group and 32.8% in the supine group (P<0.001). The hazard ratio for death with prone positioning was 0.39 (95% CI, 0.25 to 0.63). Unadjusted 90-day mortality was 23.6% in the prone group versus 41.0% in the supine group (P<0.001), with a hazard ratio of 0.44 (95% CI, 0.29 to 0.67). The incidence of complications did not differ significantly between the groups, except for the incidence of cardiac arrests, which was higher in the supine group.

Conclusions

In patients with severe ARDS, early application of prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality.

OTHER

Massachusetts General Hospital Prone Positioning for Non-Intubated Patients Guideline[15]

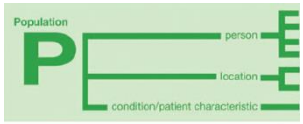
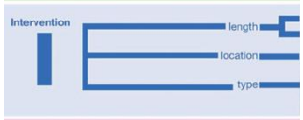
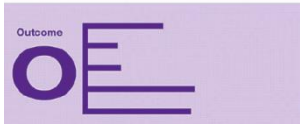
For patients with hypoxemia, there are many physiologic benefits to the prone, as opposed to the supine, position. These include better matching of pulmonary perfusion to ventilation, better recruitment of dependent areas of the lung and improved arterial oxygenation. In addition, there is evidence that the prone position results in a more homogenous distribution of stresses in the lung and thus may prevent patients with hypoxemia from developing frank respiratory failure. Prone positioning is extensively used in the ICU to treat intubated patients with hypoxemic respiratory failure1,2, but the benefits cited above should accrue to non-intubated patients as well. For this reason, patients admitted with hypoxemia should be encouraged to adopt the prone position where practical and prone positioning may be used as a rescue therapy in patients with escalating oxygen needs. This document serves to inform clinicians about prone positioning of non-intubated, hypoxemic patients.

PulmCrit (2016) [Blog]. Proning the non-intubated patient[16]

Prone positioning has been shown to improve oxygenation and survival among intubated patients with ARDS. Scaravilli et al[13] proves that proning awake patients will similarly improve their oxygenation, although this improvement is only temporary. Proning awake patients may occasionally be a useful technique to recruit the lung bases, improve oxygenation and promote secretion clearance. Among patients with hypoxemic respiratory failure, it remains unclear which patients could be treated with noninvasive techniques such as high-flow nasal cannula and awake proning versus which patients should be intubated. If noninvasive techniques are attempted, this should be done with intensive monitoring and the ability to intubate promptly if necessary.

Produced by the members of the National Health Library and Knowledge Service Evidence Team†. Current as at 28 April 2020. This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:

	COVID-19 PATIENTS RECEIVING NON-INVASIVE VENTILATION OR VENTILATING ON ROOM AIR
	PRONE POSITIONING
	
	EVIDENCE OF SAME?

The following search strategy was used:

[ABBREVIATED] COVID-19 OR CORONAVIRUS OR "CORONA VIRUS" OR (WUHAN N3 VIRUS) OR (("2019-NCOV" OR "2019 NCOV")) OR "SEVERE RESPIRATORY SYNDROME CORONAVIRUS2" OR (("2019" AND (NEW OR NOVEL) AND CORONAVIRUS)) (HCOV-19) AND (NON-INVASIVE VENTILATION) AND (PRONE POSITIONING)

† Pauline Ryan, Librarian, University Hospital Waterford [Author]; Emma Quinn, Librarian, St. Luke's General Hospital, Kilkenny [Author]; Brendan Leen, Regional Librarian, HSE South, St. Luke's General Hospital, Kilkenny [Editor].

[1] Intensive Care Society of Ireland (2020) Guidance document for the Intensive Care Management of the adult patient with confirmed or suspected COVID-19 https://www.intensivecare.ie/wp-content/uploads/2020/02/ICS-Guidelines-COVID-19-V4.pdf [Accessed 22/04/2020]
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