

2020

How I Do It: High Flow, Non-invasive ventilation and Awake (non-intubation) Proning in Covid-19 Patients with Respiratory Failure.

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Recommended Citation

Raoof S, Nava S, Carpati C, Hill N. How I Do It: High Flow, Non-invasive ventilation and Awake (non-intubation) Proning in Covid-19 Patients with Respiratory Failure.. . 2020 Jan 01; ():Article 6461 [p.]. Available from: <https://academicworks.medicine.hofstra.edu/publications/6461>. Free full text article.

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High-Flow, Noninvasive Ventilation and Awake (Nonintubation) Proning in Patients With COVID-2019 With Respiratory Failure

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The coronavirus disease 2019 pandemic will be remembered for the rapidity with which it spread, the morbidity and mortality associated with it, and the paucity of evidence-based management guidelines. One of the major concerns of hospitals was to limit spread of infection to health-care workers. Because the virus is spread mainly by respiratory droplets and aerosolized particles, procedures that may potentially disperse viral particles, the so-called “aerosol-generating procedures” were avoided whenever possible. Included in this category were noninvasive ventilation (NIV), high-flow nasal cannula (HFNC), and awake (nonintubated) proning. Accordingly, at many health-care facilities, patients who had increasing oxygen requirements were emergently intubated and mechanically ventilated to avoid exposure to aerosol-generating procedures. With experience, physicians realized that mortality of invasively ventilated patients was high and it was not easy to extubate many of these patients. This raised the concern that HFNC and NIV were being underutilized to avoid intubation and to facilitate extubation. In this article, we attempt to separate fact from fiction and perception from reality pertaining to the aerosol dispersion with NIV, HFNC, and awake proning. We describe precautions that hospitals and health-care providers must take to mitigate risks with these devices. Finally, we take a practical approach in describing how we use the three techniques, including the common indications, contraindications, and practical aspects of application.

CHEST 2020; ■(■):■-■

KEY WORDS: awake proning; coronavirus disease 2019; COVID-19; helmet mask; high-flow nasal cannula; noninvasive ventilation

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which has swept through much of the world. The disease is spread through

respiratory droplets and contact with fomites.¹ Airborne transmission has occasionally been implicated in patients with COVID-19 during procedures that are capable of generating aerosols.^{2,3}

ABBREVIATIONS: AGP = aerosol-generating procedure; COVID-2019 = coronavirus disease 2019; HEPA = high-energy particulate accumulator; HFNC = high-flow nasal cannula; NIV = noninvasive ventilation; NRB = nonrebreather; PEEP = positive end-expiratory pressure; PPE = personal protective equipment; ROX = ratio of oxygen saturation as measured by pulse oximetry/FiO₂ to respiratory rate; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SO = standard oxygen

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DOI: <https://doi.org/10.1016/j.chest.2020.07.013>

111 Approximately 5% of the patients who contract COVID-
 112 19 require admission to ICUs.⁴ They tend to be older,
 113 generally over the age of 60 years, with comorbidities
 114 such as hypertension, diabetes, cardiac disease, and
 115 obesity.^{5,6} The rate of intubation and mechanical
 116 ventilation among patients admitted to the ICU has
 117 variously been reported as 71% to 90%.⁷⁻⁹ When these
 118 patients develop hypoxemic respiratory failure, they are
 119 often on a fast track to proceed from low-flow oxygen
 120 supplementation via nasal cannula to a nonrebreather
 121 (NRB) face mask, and then directly to intubation and
 122 mechanical ventilation. The reasons for rapidly resorting
 123 to invasive mechanical ventilation include concerns that a
 124 rapid decline in respiratory status may take place, that
 125 mitigation of viral spread necessitates limiting entry to an
 126 infected patient's room, and that other respiratory
 127 modalities such as a high-flow nasal cannula (HFNC),
 128 noninvasive ventilation (NIV), and awake (nonintubated)
 129 proning may result in dispersal of viral particles in the
 130 atmosphere.¹⁰ In the presence of bilateral lung opacities
 131 and hypoxemic respiratory failure, most of the intubated
 132 patients are placed on the low tidal volume and adequate
 133 positive end-expiratory pressure (PEEP) lung-protective
 134 strategy recommended by the ARDS Network trial.¹¹

137 Among patients with COVID-19 with ARDS, Gattinoni
 138 et al¹²⁻¹⁴ have described an "L" phenotype (for low
 139 elastance) among patients who demonstrate relatively
 140 preserved respiratory system compliance of > 50 mL/cm
 141 H₂O with focal areas of ground-glass opacity on CT
 142 scanning. In contrast, others manifest the low
 143 compliance ("H" phenotype—for high elastance) that is
 144 typically seen in non-COVID-19 patients with ARDS.

147 The concerns about aerosol dispersion have led to calls
 148 for early intubation,¹⁵ leading many hospitals to
 149 discourage use of noninvasive modalities. A significant
 150 number of patients with COVID-19-induced
 151 pneumonia and ARDS could avoid invasive mechanical
 152 ventilation and its attendant risks of ventilator-induced
 153 lung injury^{5,7,16} and health care-acquired pneumonia.¹⁷
 154 In this article, we discuss the potential role of HFNC,
 155 NIV (including helmet), and awake proning in the
 156 management of COVID-19-induced acute respiratory
 157 failure. We enumerate the indications, contraindications
 158 and "How I Do It" techniques, in the context of the
 159 limited but emerging safety data available.

163 High-Flow Nasal Cannula

164 HFNC refers to high-flow oxygenated gas, heated and
 165 humidified to body conditions, that is delivered via nasal

cannula at maximum flows ranging from 40 to 80 L/min
 depending on the manufacturer.¹⁸ It has not been
 around for as long as NIV, having gained traction over
 the past 8 years or so. The heating and humidification
 make it tolerable; a dry cool gas at those flow rates would
 rapidly desiccate the nasal mucosa, causing an
 uncomfortable burning sensation. Also enhancing
 tolerability is the soft, loosely fitting nasal interface that
 does not impede speech or eating during use. The heat
 and humidification also help to maintain hydration and
 mobility of secretions and to preserve mucociliary
 function. HFNC helps with oxygenation by flushing the
 nasopharynx during exhalation so that the first bolus of
 air during inspiration is not just expired air but is partly
 freshened by the oxygenated HFNC gas. Also, compared
 with standard oxygen (SO) techniques, the high flow
 rate of HFNC comes closer to the inspiratory flow rates
 encountered in dyspneic patients, which may exceed 60
 L/min. For example, the NRB mask provides oxygen
 flows up to only 15 L/min, so that air entrainment and
 dilution of F_{IO₂} is greater than with HFNC. The flushing
 of the nasopharynx also washes out anatomic dead
 space, improving ventilatory efficiency. That, and the
 reduction in respiratory rate probably caused by the
 slowing of exhalation by the inflowing gas, contribute to
 a reduction in work of breathing per minute. The
 expiratory impedance also creates positive expiratory
 pressure that peaks early during exhalation, amounting
 to roughly 1 cm H₂O/10 L/min high flow and has been
 shown to increase end-expiratory lung volume. Thus,
 HFNC is more than just oxygen supplementation; it is a
 very well-tolerated ventilatory assist device with multiple
 potentially advantageous physiologic attributes that is
 also easy and safe to apply.

166 Physiologic Comparison With NIV

167 HFNC is primarily a flow generator and it is via high
 168 flow that it achieves its main beneficial effects of more
 169 reliably delivering a targeted F_{IO₂} than standard oxygen
 170 supplementation (although in a clinical setting, accurate
 171 measurement of actual F_{IO₂} delivered to the lungs is
 172 currently not possible) and reducing dead space to
 173 improve ventilatory efficiency. NIV, in contrast, is
 174 primarily a pressure-targeted modality, and it is pressure
 175 that is responsible for its success for its two main
 176 indications. These include acute respiratory failure in
 177 COPD exacerbations by counterbalancing intrinsic
 178 PEEP with external PEEP and providing pressure
 179 support to assist inhalation,¹⁹ and in acute cardiogenic
 180 pulmonary edema by applying CPAP or bilevel PAP to

TABLE 1] Recommendations of International Societies Regarding Use of High-Flow Nasal Cannula and Noninvasive Ventilation in COVID-19 Pandemic

Organization/Country	HFNC		NIV	
	Recommendation	Comment	Recommendation	Comment
Asociación Argentina de Medicina Respiratoria, Argentina	PRO	Nasal prongs tight to minimize aerosol	PRO	Short trial (1 h)
Australian National COVID-19 Clinical Evidence Taskforce, Australia	None	None	CONTRA	Consider only with concomitant COPD with type 2 respiratory failure or CPE
Australian and New Zealand Intensive Care Society (ANZICS), Australia and New Zealand	Suggest	None	Not routine	None
Austrian ICU therapy guideline for the treatment of patients with SARS-CoV-2 infection, Austria	No mention	None	CONTRA	Consider short trial <i>only</i> if HFNC is not feasible
Associação Brasileira de Fisioterapia Cardiorrespiratória e Fisioterapia em Terapia Intensiva, Brazil	No mention	None	PRO (conditional)	In certain situations a short trial (30 min)
Canadian Critical Care Society, Canada	None	None	PRO (conditional)	In certain situations a short trial (30 min)
Sociedad Chilena de Kinesiología Respiratoria, Chile	None	None	PRO (conditioned)	Short trial <i>only</i> if HFNC is not feasible. Helmet suggested
Chinese National Health Commission, China	None	None	PRO	Short trial (1 h)
German recommendations for critically ill patients with COVID-19, Germany	Restrictive	None	Restrictive	Only in patients with P/F > 200; helmet suggested
Irish Thoracic Society, Ireland	PRO	HFNC 30 L/min in negative-pressure room	PRO	Helmet suggested
Italian Thoracic Society and Italian Respiratory Society, Italy	None	None	PRO	None
Société Libanaise de Pneumologie, Lebanese; Society of Critical Care Medicine, Lebanese; Society of Anesthesiologists, Lebanon	CONTRA	Favor early intubation	CONTRA	None
Pakistan Chest Society, Pakistan	Conditional	If in negative-pressure room	CONTRA	None
Sociedade Portuguesa de Pneumologia, Portugal	No mention	None	Conditional	Short trial (1 h) Facial mask suggested
Sociedad Española de Neumología y Cirugía Torácica, Spain	PRO	Maintain > 2-m distance	PRO	None
Swiss Academy of Medical Sciences, Switzerland	None	None	CONTRA	Eventually only in the ICU
National Health Care System guidelines, UK	CONTRA	No benefit but risk	PRO	CPAP for mild hypoxia and NIV for acute or chronic respiratory failure
American College of Chest Physicians, USA	None	None	Careful use	The recommendations are only for home-based ventilated patients

(Continued)

TABLE 1] (Continued)

Organization/Country	HFNC		NIV	
	Recommendation	Comment	Recommendation	Comment
World Health Organization interim guidance, January 2020	Selected	Not for COPD, CPE, hemodynamic instability	Selected use	None
US Department of Defense COVID management guidelines	PRO	None	CONTRA	Early intubation over NIV if HFNC fails
US Surviving Sepsis Campaign/SCCM guidelines	Suggest ^a	HFNC next modality in those not tolerating supplemental O ₂	None	Suggest if HFNC unavailable or patient is not tolerating it

CONTRA = against; COVID-19 = coronavirus disease 2019; CPE = cardiogenic pulmonary edema; HFNC = high-flow nasal cannula; NIV = noninvasive ventilation; P/F = PaO₂/FiO₂ ratio; PRO = for; SARS-CoV-2 = severe acute respiratory syndrome coronavirus type 2; SCCM = Society of Critical Care Medicine.

^aHFNC not considered an aerosol-generating procedure.

increase functional residual capacity, which improves oxygenation and lung compliance.²⁰

Evidence for Efficacy

A number of studies have compared HFNC with NIV and SO. HFNC has been shown to be more comfortable and better tolerated than either.¹⁸ It provides better oxygenation as compared with SO^{21,22}; however, it is not as good an oxygenator as NIV, presumably because mean airway pressure is less. Randomized clinical trials comparing the clinical efficacy of these various approaches with noninvasively supporting patients with acute hypoxemic respiratory failure are very few. Frat et al²³ compared HFNC (50 L/min; FiO₂, 100%) with SO using an NRB mask (≥ 10 L/min), and with NIV using pressure support to achieve a tidal volume of 7 to 10 mL/kg ideal body weight. The major outcome variable, intubation rate, was 38%, 47%, and 50% in the three groups, respectively, which was not statistically significant. However, there was a significant drop in intubation rate in the HFNO group compared with the SO and NIV groups in the subgroup of patients with PaO₂/FiO₂ < 200. Mortality was also significantly less in the HFNO group than the others in the ICU and after 90 days (30%, 45%, and 49%, respectively).²³ Other randomized studies have demonstrated that HFNC is noninferior to NIV in patients at risk for reintubation after cardiac surgery²⁴ and after extubation following a bout of acute respiratory failure.²⁵ It also reduced the reintubation rate compared with SO in lower risk respiratory failure patients after extubation.²⁶ One recent study showed that the combination of HFNC alternating with NIV in postextubation patients reduced

the reintubation rate more than with HFNC alone.²⁷ Thus, HFNC offers a number of advantages over SO and NIV as well as some limitations, but should be a first-line consideration when patients with COVID-19 pneumonia are mildly to moderately hypoxemic.

The Controversy

As reflected by the varying recommendations in the guidelines offered by various eminent organizations, HFNC for the management of COVID-19 pneumonia has been very controversial (Table 1). Some guidelines caution against the routine use of HFNC or any noninvasive, potentially aerosol-generating approach²⁸; others, such as the Surviving Sepsis/Society of Critical Care Medicine guideline,²⁹ advocate it as a first-line approach. Some hospitals strongly discourage the use of noninvasive approaches, favoring early intubation, and others use noninvasive approaches quite commonly. The contention is that failure rates of noninvasive approaches in patients with COVID are high, and these are aerosol-generating procedures (AGPs) that place caregivers at increased risk of contracting COVID-19. The contrary view is that aerosol-mitigating interventions such as the use of negative-pressure rooms, high-energy particulate accumulator (HEPA) filters, and adequate personal protective equipment (PPE) are sufficient to protect staff. In addition, the noninvasive approaches will avoid unneeded intubations that are well-known generators of considerable amounts of aerosol, thus protecting staff. Avoidance of intubation might improve patient outcomes and preserve much-needed critical care ventilators that have been in short supply in “hot spot” areas. There are a number of studies

that have examined aerosol dispersion during use of various AGPs that, regarding HFNC, have been reassuring. These show a smaller distance of dispersion for HFNC than for a number of other AGPs,³⁰⁻³² but because most have been performed with human mannequins with smoke or some other substitute particulate, they have not universally allayed the concerns of some practitioners. A recent study suggests that a droplet (surgical) mask placed over the nasal interface can greatly reduce dispersion of aerosol.³³ Another recent study of healthy volunteers showed no increase in aerosol over background in a simulated hospital room with HFNC up to maximal flow rates of

60 L/min, compared with use of a standard nasal cannula or an NRB mask.³⁴

Indications and Application for HFNC in Patients With COVID-19

Figure 1 and Tables 2 and 3 summarize the indications, contraindications, and technique for performing HFNC, NIV, and awake proning. HFNC is a better tolerated and more efficacious alternative to the NRB mask when standard nasal prongs are deemed insufficient. This would have been the preferred initial choice at many centers in the United States. HFNC is likely to be better tolerated than NIV with an orofacial mask or the helmet

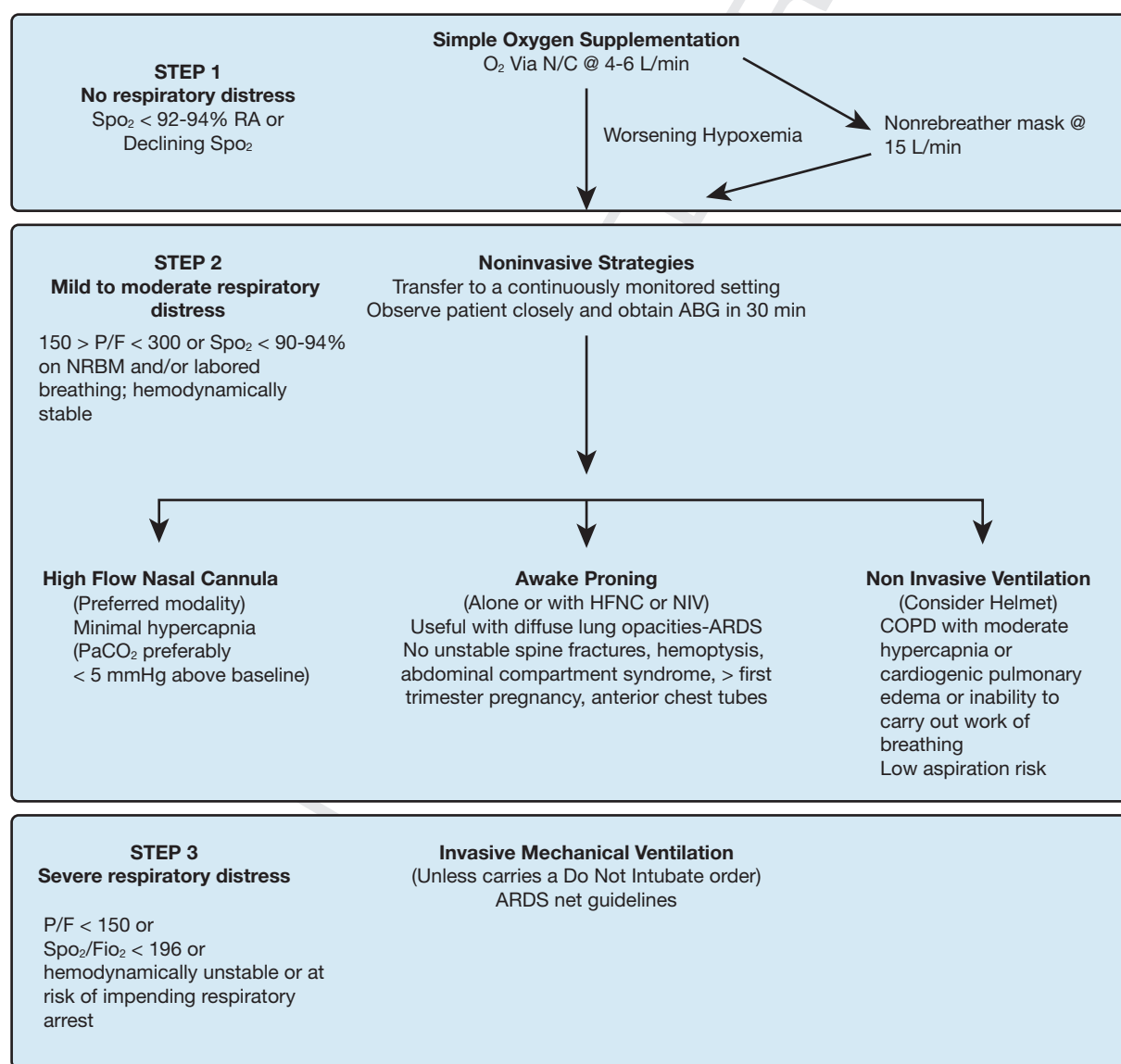


Figure 1 – Algorithmic approach to respiratory failure in coronavirus disease 2019. ABG = arterial blood gas; HFNC = high-flow nasal cannula; N/C = nasal cannula; NIV = noninvasive ventilation; NRBM = nonrebreathing reservoir mask; P/F = PaO₂/Fio₂ ratio; RA = room air; SpO₂ = arterial oxygen saturation as determined by pulse oximetry.

and may also facilitate the use of proning. To our knowledge there are not, at present, any head-to-head trials comparing HFNC with the helmet, but we have seen some patients fail to oxygenate adequately with HFNC and go on to improve with the helmet, presumably because of the helmet's greater positive airway pressure. On the other hand, we have seen HFNC succeed when the helmet fails, mainly because of patients' better tolerance of HFNC. Expense is greater for HFNC over nasal cannula but not inordinately so

(\$85.75 including interface, circuit, and water bag for HFNC vs \$0.33 for nasal cannula at a hospital in New York City).

HFNC Failure

The greatest danger when using HFNC, especially with patients with COVID-19, is to fail to monitor closely enough, leading to an unanticipated need for intubation with increased risk to the patient of respiratory arrest and increased risk of aerosol exposure to the intubating

TABLE 2] Physiologic Effects, Indications, and Recommended Precautions With High-Flow Nasal Cannulas, Noninvasive Ventilation, and Awake Proning

	HFNC	Awake Proning	NIV ± Helmet
Physiologic effects	<ul style="list-style-type: none"> Heated, humidified high-flow, high F_{iO_2} Flushes nasopharynx with O_2 in exhalation; improves oxygenation and reduces dead space Reduces WOB Expiratory impedance generates extrinsic PEEP of 4-6 cm H_2O and lowers respiratory rate Heating and humidification of gases preserve mucociliary clearance 	<ul style="list-style-type: none"> Reduces alveolar overdistension in the nondependent areas as well as collapse of alveoli in dependent areas, improving \dot{V}/\dot{Q} and shunt Less compression of dorsal regional lung units with maintenance of dorsal perfusion improves \dot{V}/\dot{Q} matching May facilitate drainage of respiratory secretions from dorsal lung regions Ventilation more homogeneous 	<ul style="list-style-type: none"> Augments tidal volume (bilevel PAP) Improves alveolar ventilation and lowers P_{aCO_2} Counters intrinsic PEEP Increases end-expiratory volume and opens atelectatic lung units Generates higher mean airway pressures; hence improves P_{aO_2} Reduces WOB
Indications	<p><i>For incipient respiratory failure:</i></p> <ul style="list-style-type: none"> Usually first-line treatment if simple O_2 supplementation is insufficient <p><i>In postextubation patients:</i></p> <ul style="list-style-type: none"> After prolonged bouts of invasive mechanical ventilation (reduced WOB) If weakness is profound, alternate NIV and HFNC every couple of hours (NIV for greater ventilatory assistance; HFNC for better tolerance and humidification) Marginal oxygenation status (Sp_{O_2} high 80s or low 90s) Thick secretions (improved hydration) 	<ul style="list-style-type: none"> May be used alone or in combination with HFNC or NIV May be tried cautiously in patients who are significantly more hypoxemic than those recruited for HFNC or NIV More likely to be useful in patients with diffuse lung opacities 	<p><i>For incipient respiratory failure:</i></p> <ul style="list-style-type: none"> COPD exacerbation with hypercapnic respiratory failure Cardiogenic pulmonary edema Greater inspiratory pressure provision for patients failing HFNC <p><i>In postextubation patients:</i></p> <ul style="list-style-type: none"> Same indications as for incipient respiratory failure above Often combined with HFNC
Precautions	<ul style="list-style-type: none"> Very rarely, patient may not tolerate Some patients develop facial abrasions from self-proning ROX ($[Sp_{O_2}/F_{iO_2}]/RR$) score ≤ 3.85 at 12 h may predict failure 	<ul style="list-style-type: none"> Use pillows under pressure points After proning, copious secretions may drain Patients with fresh tracheostomy, anterior chest wall thoracostomy tubes, hemoptysis, cardiac arrhythmias, unstable spine fractures, abdominal compartment syndrome, and > 1st trimester of pregnancy should generally not be placed in prone position 	<ul style="list-style-type: none"> Claustrophobia Aspiration risk Continued recruitment of accessory muscles Generation of excessive tidal volumes (self-induced lung injury) In patients with P/F < 150 NIV may be associated with increased mortality compared with invasive ventilation

PAP = positive airway pressure; PEEP = positive end-expiratory pressure; ROX = ratio of oxygen saturation as measured by pulse oximetry/ F_{iO_2} to respiratory rate; RR = respiratory rate; WOB = work of breathing. See Table 1 legend for expansion of other abbreviations.

TABLE 3] How I Do It: Technique and Monitoring of High-Flow Nasal Cannula, Noninvasive Ventilation, and Awake Proning

	HFNC	Awake Proning	NIV ± Helmet
Technique	<ul style="list-style-type: none"> • Use in a negative-pressure room if available; if not, ask for a room with at least 6 (preferably 12) air exchanges/h, along with a HEPA filter • Fit nasal prongs, using fitting guides per manufacturer • Strap on firmly but not too tightly to nostrils • Initiate flow near maximum for manufacturer (50 L/min [60 L/min max] used for initiation in key studies that used Fisher & Paykel equipment) • Place droplet mask over nose and nasal interface to reduce aerosol dispersion • F_{IO_2} as per oxygenation defect; if moderately severe to severe, start with 100% and adjust down to Sa_{O_2} target. If mild to moderate can start with 50% • Start with 37°C temperature and adjust down to 34°C or 31°C if needed for better tolerance 	<ul style="list-style-type: none"> • An Ambu bag and PEEP valve should be available • The judicious use of pillows positioned under the pelvis may be useful • IVs except those administering pressors should be capped off • Adequate number of staff should be present, depending on how much assistance the patient will require • One lead health-care provider should give instructions to the team to coordinate rolling the patient if needed • Vigilance should be maintained to ensure that lines and catheters do not get dislodged • Oxygenation adjuncts may become displaced during the practice of proning, with life-threatening results • Adequate tubing length should be ensured to minimize this risk 	<ul style="list-style-type: none"> • Use in a negative-pressure room • Full PPE and N-95 masks for health-care providers entering the room • Use helmet mask if feasible, or oronasal masks • Use ICU ventilator and with dual circuitry and with NIV option, if available • Use filter on expiratory limb • Assisted time control mode of ventilation • Initiate with CPAP of 10 cm and PSV 15 and titrate to $RR < 20/min$ • F_{IO_2} at 1.0 and titrate to maintain $Sp_{O_2} > 92\%$
Monitoring	<ul style="list-style-type: none"> • Monitor RR and breathing pattern • Check ABG in $1/2$ h • May consider alternating with NIV or using awake proning to improve oxygenation further 	<ul style="list-style-type: none"> • Once proning is completed, it is recommended that the patient be observed closely • Some require suctioning • Some may show desaturation • Of note, those patients who show an improvement in Sp_{O_2} usually do so in the first 2 h • In individual circumstances, mild sedation or anxiolysis may be considered • Close monitoring of vital signs and oxygenation must be performed 	<ul style="list-style-type: none"> • Stay at patient's bedside and observe RR and improvement in breathing • Check ABG in $1/2$ h • Adjust CPAP and PSV to improve Sp_{O_2} and lower RR • Check delivered tidal volumes with above pressures • Can use small doses of sedatives, if needed • Can use thin-bore feeding tube for nasogastric tube feeding, unless there is a contraindication

ABG = arterial blood gas; HEPA = high-energy particulate accumulator; PPE = personal protective equipment; PSV = pressure support ventilation; Sa_{O_2} = oxygen saturation. See Table 1 and 2 legends for expansion of other abbreviations.

team. Thus, it is important to have patients at risk for progression in a closely monitored setting such as an ICU or intermediate care unit. Indicators of impending failure include increasing tachypnea and tachycardia, failure to adequately support oxygenation despite a high flow rate and F_{IO_2} , a climbing $Paco_2$ in a struggling patient, development of dyssynchronous breathing, alteration in mental status, and hemodynamic instability. In some patients who are not too unstable, a trial of NIV may be worthwhile, but it is important to intubate before a crisis occurs. Recently, the ROX index has been suggested as a way of predicting impending failure of HFNC. This consists of calculating (oxygen saturation [Sa_{O_2}]/ F_{IO_2})/respiratory rate (RR), thus

incorporating an index of gas exchange with another of breathing effort. Roca et al³⁵ reported that an ROX score > 4.88 at 12 h predicted success of HFNC with an area under the curve of 0.75. An ROX score ≤ 3.85 at 12 h predicted failure with nearly 100% specificity.

Summary

HFNC is very simple and safe to apply and is a favorite of respiratory therapists for that reason. Relevant to caregivers, patients tend to leave the HFNC prongs in place more than is the case with mask oxygen or NIV, reducing the number of needed visits into the room. The major precautions that should be exercised in its application are related to putting an HFNC on unstable

771 or severely hypoxemic patients and not monitoring
772 them adequately. This may culminate in severe
773 hypoxemia and an emergency intubation. This is
774 catastrophic because it takes minutes for the code and
775 intubation teams to apply appropriate PPE, and
776 intubation is a high-risk AGP, not to mention the
777 greater risk of morbidity and mortality to the patient.
778

780 Noninvasive Positive-Pressure Ventilation 781 With Helmet

782 *Description of Technique*

784 NIV is a well-established technique that has gained
785 popularity in the last 30 years.³⁶ Usually NIV is
786 delivered by critical care ventilators for severely hypoxic
787 patients. These ventilators allow the option of setting
788 F_{iO_2} through a blender, permit visualization of waveform
789 displays, and allow separate inspiratory and expiratory
790 circuits. By placing a fixed exhalation valve, filtering in a
791 closed system reduces aerosol dispersion, features not
792 always available in dedicated NIV platforms that have a
793 single circuit and a fixed exhalation valve.³⁷ Filters can
794 be attached to the exhalation valve with some NIV
795 platforms, which may reduce contamination of the
796 environment.
797

799 Spontaneous modes are generally used with NIV to
800 enhance synchrony and comfort. Therefore, deep
801 sedation cannot be used for safety reasons. This limits
802 the use of NIV only in mildly to moderately hypoxemic
803 patients, because volume-targeted ventilation is not
804 feasible.
805

806 In clinical practice, pressure support ventilation,
807 together with the addition of external PEEP, is virtually
808 the only mode used.
809

810 At present, most ICU ventilators have the so-called NIV
811 option, which is able to better compensate for the
812 unavoidable leaks with NIV.³⁸
813

814 Concerning the interfaces recommended, most studies
815 have used full or total face masks, whereas for
816 pandemics the European Respiratory Society/European
817 Society of Intensive Care Medicine (ERS/ESICM) has
818 suggested the use of the helmet for safety reasons (see
819 below). During the COVID-19 outbreaks, the Italian
820 societies strongly recommended use of the helmet.^{39,40}
821 When applying this interface, the specific settings used
822 are different than with an oronasal (full face) mask. The
823 “usual” inspiratory and expiratory pressures used to
824 deliver NIV through an oronasal mask are increased by
825 50% and the fastest pressurization rate is applied.⁴¹

826 Examples would be PEEP of 8 to 12 cm H_2O and
827 pressure support of 12 to 20 cm H_2O .
828

829 *Safety and Precautions*

830 As illustrated in [Table 1](#), some international societies do
831 not recommend the use of NIV for COVID-19
832 treatment. These suggestions are driven by concerns
833 about dispersion and the stability of COVID-19 in
834 clinical spaces. World Health Organization guidelines
835 for the management of respiratory failure in COVID-19
836 do advocate, however, the use of CPAP or NIV,
837 provided that appropriate PPE is worn.²⁸
838

839 On the basis of a recent review of the literature on
840 maximum exhaled air dispersion via different oxygen
841 administration and ventilatory support strategies, we
842 have concluded that CPAP via an oronasal mask and
843 NIV via a helmet equipped with an inflatable neck
844 cushion are the ventilatory support methods that allow
845 minimum room air contamination; less than with every
846 other oxygen delivery system.⁴²
847

849 These studies were conducted with a human simulator
850 device in a negative-pressure room with at least six air
851 exchanges per hour (minimum air changes per hour
852 recommended by the World Health Organization is 12).
853 In medical wards not equipped with negative-pressure
854 rooms, higher exhaled air dispersion and contamination
855 are likely, so the use of a HEPA filter is recommended. If
856 negative-pressure rooms are not available, rooms with
857 natural ventilation with airflow of at least 160 L/s per
858 patient is recommended.
859

860 *Indications*

861 The most recent European Respiratory Society/
862 American Thoracic Society (ERS/ATS) guidelines made
863 no recommendation for or against the use of NIV during
864 a pandemic, due to insufficient evidence, but they do
865 state that during pandemics a trial of NIV could be
866 considered in carefully selected patients at experienced
867 centers in a protected environment.⁴³ However, further
868 research is needed before this could be recommended.
869

870 Discouraging NIV in the COVID-19 pandemic may
871 increase the need for intubation and lead to increased
872 morbidity and mortality and decreased ventilator
873 availability, especially in those geographical areas hit
874 hard by the pandemic.
875

877 Observational studies showed that NIV or CPAP may
878 stabilize the clinical course of a patient with mild to
879 moderate acute respiratory failure due to COVID-19,
880 provided the patient does not demonstrate a high

881 inspiratory drive or exert excessive inspiratory efforts.^{5,8}
 882 Caveats would include careful patient selection so as not
 883 to delay intubation where appropriate.
 884

885 In an observational study of 459 ICU patients from 50
 886 countries, Bellani et al⁴⁴ demonstrated that NIV was
 887 used in real life in about 15% of patients with ARDS,
 888 irrespective of severity of disease. However, NIV was
 889 associated with higher ICU mortality in patients with a
 890 $\text{PaO}_2/\text{FiO}_2$ ratio less than 150 mm Hg, suggesting that the
 891 “potential” target for a cautious NIV trial may be above
 892 this $\text{PaO}_2/\text{FiO}_2$ ratio.
 893

894 Observing patients for 1 to 2 hours after instituting NIV
 895 is important. An increasing respiratory rate and
 896 recruitment of accessory muscles use would indicate
 897 high work of breathing, suggesting the need for
 898 intubation.⁴⁶ In conclusion, a cautious NIV trial may be
 899 indicated in a subset of patients with mild to moderate
 900 acute respiratory failure, using interfaces that minimize
 901 droplet dispersion (ie, the helmet) in negative-pressure
 902 rooms or even in a space with sufficient airflow, and
 903 protecting the personnel with personal protective
 904 equipment.
 905

907 Awake Proning

908 Background

909 First described in the 1970s in both intubated and
 910 spontaneously breathing patients,⁴⁷ the use of prone
 911 positioning has become a mainstay tool to ameliorate
 912 physiology and survival in hypoxemic respiratory failure
 913 requiring mechanical ventilation associated with ARDS.
 914 Although the frequent beneficial effects on hypoxemia
 915 are touted, the survival benefit in mechanically
 916 ventilated patients is independent of the improvement in
 917 arterial oxygen saturation.⁴⁸ As the availability of both
 918 invasive and noninvasive adjuncts for mechanical
 919 ventilation may not meet demand in a pandemic, and
 920 the avoidance of invasive mechanical ventilation may
 921 itself be beneficial, the concept of proning in
 922 spontaneously breathing patients has been reexplored in
 923 small studies, attaining more urgency with the COVID-
 924 19 pandemic.
 925

926 Evidence

927 Although there have been few studies and case reports in
 928 the nonintubated population with hypoxemic
 929 respiratory failure, and the total number of patients
 930 included is relatively small, the results of these studies
 931 have been uniformly positive. In the pre-COVID era,
 932 Scaravilli et al⁴⁹ reported retrospective data confirming
 933

934 improvement in oxygenation during prone positioning
 935 in patients receiving oxygen or noninvasive ventilation
 936 modalities with moderate to severe hypoxemic
 937 respiratory failure. The improvement was reversed on
 938 resupination. Ding et al⁵⁰ reported a series of 20
 939 nonintubated patients with moderate to severe ARDS
 940 treated with HFNC or NIV who underwent a mean of
 941 approximately two proning sessions per day for an
 942 average of 2 hours each. Most of the patients
 943 experienced improved oxygenation, and intubation was
 944 avoided in 11 of the patients.
 945

946 In the nascent COVID-19 era, Caputo et al⁵¹ have
 947 reported their ED experience using awake self-proning
 948 for 50 consecutive patients with COVID-19 with $\text{SpO}_2 <$
 949 93% on supplemental oxygen, excluding patients
 950 requiring NIV. The median SpO_2 on supplemental
 951 oxygen therapy improved from 84% to 94% after 5 min
 952 of self-proning; seven of the patients did require
 953 endotracheal intubation within 60 min of the
 954 intervention. In a case series of 24 patients, Elharrar
 955 et al⁵² found that 63% of patients tolerated 3 hours or
 956 more of proning and 25% had a $> 20\%$ increase in PaO_2
 957 but returned toward baseline on resupination. In
 958 another case series of 15 patients receiving NIV in the
 959 prone position for a median of two cycles with a total
 960 duration of 3 hours, Sartini et al⁵³ found improvements
 961 in $\text{PaO}_2/\text{FiO}_2$ ratio and SpO_2 that were sustained 60 min
 962 after pronation in 80% of the patients. All patients
 963 experienced a decrease in respiratory rate and most felt
 964 an improvement in comfort. In a retrospective study by
 965 Xu et al,⁵⁴ 10 patients with diagnosed COVID-19
 966 infection and $\text{P}/\text{F} < 300$ were given early awake proning
 967 for more than 16 hours per day combined with HFNC.
 968 None of these patients required invasive mechanical
 969 ventilation and all survived. The authors proposed the
 970 concept of using early prone positioning with HFNC as
 971 a concept to, “reduce the proportion of severe COVID-
 972 19 conversion to critical illness.”
 973

974 Guidelines

975 There are no formal guidelines for proning
 976 nonintubated patients. Patients are frequently
 977 advised to remain prone for as long as tolerated.
 978 However, protocolization may improve compliance
 979 and provide a time frame that may be helpful.
 980 Suggestions include having the patient vary their
 981 position every 2 hours among prone, left and right
 982 lateral decubitus, and supine positions. Provision of
 983 an informational flyer to the patient may be of use
 984 in promoting compliance.
 985

991 In our experience, lack of compliance may be
 992 encountered in obese patients and those with a history
 993 of back pain. For these patients it may be helpful to start
 994 with shorter intervals of time and to provide a team to
 995 help with positioning. Multiple mattress adjuncts have
 996 been proposed that may help adaptation.

998 Precautions

1000 Caution and vigilance must be exercised in all prone
 1001 patients. Optimal timing in this position remains
 1002 unknown. It may be tempting and useful in individual
 1003 circumstances to aid compliance with the use of mild
 1004 sedation or anxiolysis, but this cannot be advocated
 1005 without close monitoring of vital signs and oxygenation.
 1006 Oxygenation adjuncts may become displaced during the
 1007 practice of proning, with life-threatening results.
 1008 Although the development of pressure ulcers is unlikely
 1009 in the awake prone patient, provision of appropriate
 1010 padding to pressure points such as shoulders and knees
 1011 should be considered. The judicious use of pillows
 1012 positioned under the pelvis may be useful. Finally, the
 1013 improvement in oxygenation may be transient or lead to
 1014 a false sense of security, delaying a potentially life-saving
 1015 conversion to invasive mechanical ventilation.

1017 To exemplify the clinical application of these modalities,
 1018 we present an illustrative case in [e-Appendix 1](#).

1021 Conclusions

1022 Patients with COVID-19 frequently develop pulmonary
 1023 involvement resulting in hypoxemic respiratory failure.
 1024 The prior dictum of progressing from nasal cannula to
 1025 nonrebreather face mask and then to invasive
 1026 mechanical ventilation is applicable to the majority of
 1027 these patients. However, there may be approximately
 1028 20% to 25% of patients with COVID-19 in whom
 1029 modalities such as high-flow nasal cannula therapy,
 1030 noninvasive ventilation, and awake proning may
 1031 stabilize their respiratory status and obviate the need for
 1032 intubation. Similarly, a fraction of recently extubated
 1033 patients, who are demonstrating respiratory distress or
 1034 hypoxemia, may be stabilized without needing
 1035 reintubation with these modalities. Helmet masks have
 1036 been used commonly in Italy during the COVID
 1037 pandemic with good results. There are very few data to
 1038 prove that high-flow nasal cannula and noninvasive
 1039 ventilation (especially with a helmet mask) result in
 1040 dispersion of viral particles. However, it is imperative
 1041 that when these devices are used, negative-pressure
 1042 rooms or HEPA filters along with proper PPE including
 1043 N-95 masks be used to protect health-care providers.

Acknowledgments

Financial/nonfinancial disclosures: The authors have reported to Q33 Q17
 CHEST the following: S. N. is on the advisory board for Breathe and
 has received honoraria from Philips Respironics for medical lectures.
 N. S. H. is consultant for and has received research grants to his
 institution from Fisher & Paykel. He is also a consultant and has served
 on scientific advisory boards for Philips Respironics. None declared (S.
 R., C. C.).

Other contributions: The authors acknowledge the assistance of Dr Q18
 Linda Kirschenbaum in helping to prepare the algorithm and Ms
 Patrice Balistreri for secretarial assistance.

Additional information: The [e-Appendix](#) can be found in the
 Supplemental Materials section of the online article.

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