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

S Raoof
Zucker School of Medicine at Hofstra/Northwell, sraoof@northwell.edu

S Nava

C Carpati
Zucker School of Medicine at Hofstra/Northwell, ccarpati@northwell.edu

NS Hill

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

Suhail Raoof, MD, Master FCCP; Stefano Nava, MD; Charles Carpati, MD; and Nicholas S. Hill, MD

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.

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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/F_{IO_2} to respiratory rate; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SO = standard oxygen

AFFILIATIONS: From the Lung Center, Lenox Hill Hospital, New York, NY (Drs Raoof and Carpati); Respiratory and Critical Care (Dr Nava), Sant'Orsola Malpighi Hospital, Bologna, Italy; and the Division of Pulmonary, Critical Care and Sleep Medicine (Dr Hill), Tufts Medical Center, Boston, MA.

CORRESPONDENCE TO: Suhail Raoof, MD, Master FCCP, Lung Center, Lenox Hill Hospital, and Zucker School of Medicine at Hofstra University; e-mail: suhailraoof@gmail.com

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

Among patients with COVID-19 with ARDS, Gattinoni et al[12-14] have described an "L" phenotype (for low elastance) among patients who demonstrate relatively preserved respiratory system compliance of > 50 mL/cm H_2O with focal areas of ground-glass opacity on CT scanning. In contrast, others manifest the low compliance ("H" phenotype—for high elastance) that is typically seen in non-COVID-19 patients with ARDS.

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

High-Flow Nasal Cannula

HFNC refers to high-flow oxygenated gas, heated and 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_{IO_2} is greater than with HFNC. The flushing Q8 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 H_2O/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.

Physiologic Comparison With NIV

HFNC is primarily a flow generator and it is via high flow that it achieves its main beneficial effects of more reliably delivering a targeted F_{IO_2} than standard oxygen supplementation (although in a clinical setting, accurate measurement of actual F_{IO_2} delivered to the lungs is currently not possible) and reducing dead space to improve ventilatory efficiency. NIV, in contrast, is primarily a pressure-targeted modality, and it is pressure that is responsible for its success for its two main indications. These include acute respiratory failure in COPD exacerbations by counterbalancing intrinsic PEEP with external PEEP and providing pressure support to assist inhalation,[19] and in acute cardiogenic pulmonary edema by applying CPAP or bilevel PAP to

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

Organization/Country	HFNC Recommendation	HFNC Comment	NIV Recommendation	NIV 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 *only* 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 *only* 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 = Pa_{O_2}/F_{IO_2} ratio; PRO = for; SARS-CoV-2 = severe acute respiratory syndrome coronavirus type 2; SCCM = Society of Critical Care Medicine.
[a]HFNC 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 al[23] compared HFNC (50 L/min; F_{IO_2}, 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 $Pa_{O_2}/F_{IO_2} < 200$. 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 surgery[24] 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 approach[28]; 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

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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

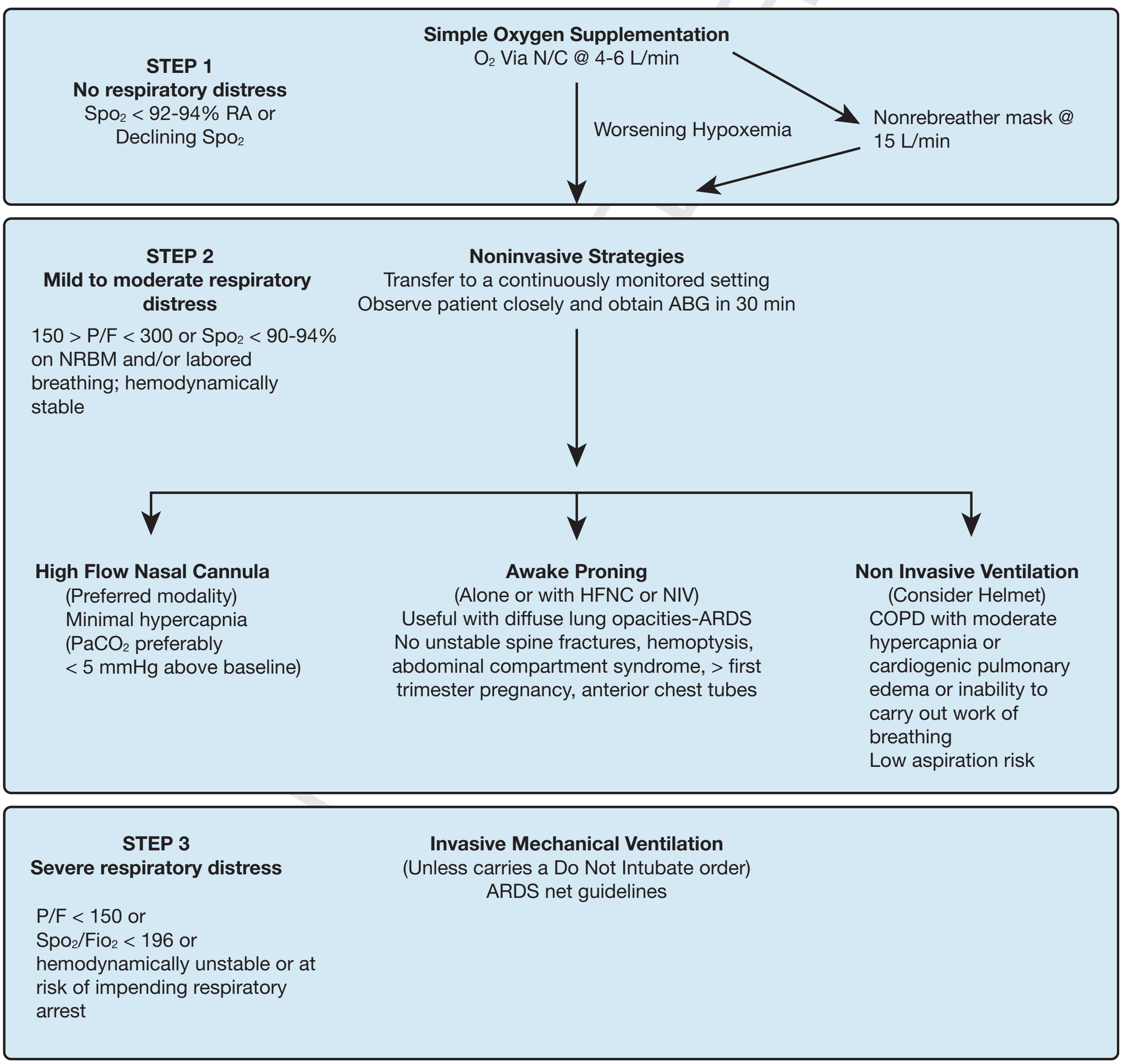

Figure 1 – *Algorithmic approach to respiratory failure in coronavirus disease 2019. ABG = arterial blood gas; HFNC = high-flow nasal cannula; N/C = nasal cannula; NIV = noninvasive ventilation; NRBM = nonrebreathing reservoir mask; P/F = Pa_{O_2}/F_{IO_2} ratio; RA = room air; Sp_{O_2} = arterial oxygen saturation as determined by pulse oximetry.*

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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	• Heated, humidified high-flow, high FIO_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	• 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	• Augments tidal volume (bilevel PAP) • Improves alveolar ventilation and lowers $PaCO_2$ • Counters intrinsic PEEP • Increases end-expiratory volume and opens atelectatic lung units • Generates higher mean airway pressures; hence improves PaO_2 • Reduces WOB
Indications	*For incipient respiratory failure:* • Usually first-line treatment if simple O_2 supplementation is insufficient *In postextubation patients:* • 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 (SpO_2 high 80s or low 90s) • Thick secretions (improved hydration)	• 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	*For incipient respiratory failure:* • COPD exacerbation with hypercapnic respiratory failure • Cardiogenic pulmonary edema • Greater inspiratory pressure provision for patients failing HFNC *In postextubation patients:* • Same indications as for incipient respiratory failure above • Often combined with HFNC
Precautions	• Very rarely, patient may not tolerate • Some patients develop facial abrasions from self-proning • ROX ([SpO_2/FIO_2]/RR) score ≤ 3.85 at 12 h may predict failure	• 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	• 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/FIO_2 to respiratory rate; RR = respiratory rate; WOB = work of breathing. See Table 1 legend for expansion of other abbreviations.

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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	• 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	• 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	• 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	• Monitor RR and breathing pattern • Check ABG in ½ h • May consider alternating with NIV or using awake proning to improve oxygenation further	• 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	• Stay at patient's bedside and observe RR and improvement in breathing • Check ABG in ½ 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 Pa_{CO_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 al[35] 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

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

Noninvasive Positive-Pressure Ventilation With Helmet

Description of Technique

NIV is a well-established technique that has gained popularity in the last 30 years.[36] Usually NIV is delivered by critical care ventilators for severely hypoxic patients. These ventilators allow the option of setting FIO_2 through a blender, permit visualization of waveform displays, and allow separate inspiratory and expiratory circuits. By placing a fixed exhalation valve, filtering in a closed system reduces aerosol dispersion, features not always available in dedicated NIV platforms that have a single circuit and a fixed exhalation valve.[37] Filters can be attached to the exhalation valve with some NIV platforms, which may reduce contamination of the environment.

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

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

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

Concerning the interfaces recommended, most studies have used full or total face masks, whereas for pandemics the European Respiratory Society/European Society of Intensive Care Medicine (ERS/ESICM) has suggested the use of the helmet for safety reasons (see below). During the COVID-19 outbreaks, the Italian societies strongly recommended use of the helmet.[39,40] When applying this interface, the specific settings used are different than with an oronasal (full face) mask. The "usual" inspiratory and expiratory pressures used to deliver NIV through an oronasal mask are increased by 50% and the fastest pressurization rate is applied.[41] Examples would be PEEP of 8 to 12 cm H_2O and pressure support of 12 to 20 cm H_2O.

Safety and Precautions

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

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

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

Indications

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

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

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

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inspiratory drive or exert excessive inspiratory efforts.[5,8] Caveats would include careful patient selection so as not to delay intubation where appropriate.

In an observational study of 459 ICU patients from 50 countries, Bellani et al[44] demonstrated that NIV was used in real life in about 15% of patients with ARDS, irrespective of severity of disease. However, NIV was associated with higher ICU mortality in patients with a Pa_{O_2}/F_{IO_2} ratio less than 150 mm Hg, suggesting that the "potential" target for a cautious NIV trial may be above this Pa_{O_2}/F_{IO_2} ratio.

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

Awake Proning

Background

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

Evidence

Although there have been few studies and case reports in the nonintubated population with hypoxemic respiratory failure, and the total number of patients included is relatively small, the results of these studies have been uniformly positive. In the pre-COVID era, Scaravilli et al[49] reported retrospective data confirming improvement in oxygenation during prone positioning in patients receiving oxygen or noninvasive ventilation modalities with moderate to severe hypoxemic respiratory failure. The improvement was reversed on resupination. Ding et al[50] reported a series of 20 nonintubated patients with moderate to severe ARDS treated with HFNC or NIV who underwent a mean of approximately two proning sessions per day for an average of 2 hours each. Most of the patients experienced improved oxygenation, and intubation was avoided in 11 of the patients.

In the nascent COVID-19 era, Caputo et al[51] have reported their ED experience using awake self-proning for 50 consecutive patients with COVID-19 with $Sp_{O_2} <$ 93% on supplemental oxygen, excluding patients requiring NIV. The median Sp_{O_2} on supplemental oxygen therapy improved from 84% to 94% after 5 min of self-proning; seven of the patients did require endotracheal intubation within 60 min of the intervention. In a case series of 24 patients, Elharrar et al[52] found that 63% of patients tolerated 3 hours or more of proning and 25% had a $>$ 20% increase in Pa_{O_2} but returned toward baseline on resupination. In another case series of 15 patients receiving NIV in the prone position for a median of two cycles with a total duration of 3 hours, Sartini et al[53] found improvements in Pa_{O_2}:F_{IO_2} ratio and Sp_{O_2} that were sustained 60 min after pronation in 80% of the patients. All patients experienced a decrease in respiratory rate and most felt an improvement in comfort. In a retrospective study by Xu et al,[54] 10 patients with diagnosed COVID-19 infection and P/F $<$ 300 were given early awake proning for more than 16 hours per day combined with HFNC. None of these patients required invasive mechanical ventilation and all survived. The authors proposed the concept of using early prone positioning with HFNC as a concept to, "reduce the proportion of severe COVID-19 conversion to critical illness."

Guidelines

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

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

Precautions

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

To exemplify the clinical application of these modalities, we present an illustrative case in e-Appendix 1.

Conclusions

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

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Additional information: The e-Appendix can be found in the Supplemental Materials section of the online article.

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