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A Rationale for Use of High Flow Nasal Cannula for Select Patients With Suspected or Confirmed Severe Acute Respiratory Syndrome Coronavirus-2 Infection

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Abstract

Infection with the novel 2019 coronavirus (SARS-CoV-2) is associated with the development of a viral pneumonia with severe hypoxemia and respiratory failure. In many cases these patients will require mechanical ventilation; but in others the severity of disease is significantly less and may not need invasive support. High flow nasal cannula (HFNC) is a widely used modality of delivering high concentrations of oxygen and airflow to patients with hypoxemic respiratory failure, but its use in patients with SARS-CoV-2 is poorly described. Concerns with use of HFNC have arisen including aerosolization of viral particles to healthcare workers (HCW) to delaying intubation and potentially worsening of outcomes. However, use of HFNC in other coronavirus pandemics and previous experimental evidence suggest HFNC is low risk and may be effective in select patients infected with SARS-CoV-2. With the significant increase in resource utilization in care of patients with SARS-CoV-2, identification of those that may benefit from HFNC allowing allocation of ventilators to those more critically ill is of significant importance. In this manuscript, we review pertinent literature regarding the use of HFNC in the current SARS-CoV-2 pandemic and address many concerns regarding its use.

Keywords

high flow nasal cannula, SARS-CoV-2, acute respiratory distress syndrome, aerosolization, critical care

Introduction

High flow nasal cannula therapy (HFNC) is a widely used modality that can deliver high concentrations of oxygen and airflow to patients with hypoxemia. It is able to deliver these high flows by heating and humidifying the gas prior to delivering it to the cannula interface. The main indication for HFNC is hypoxemic normocapnic respiratory failure, but this modality has been successfully used in other conditions or clinical scenarios such as: hypercapnic respiratory failure, support during rapid sequence intubation, weaning after extubation and in palliative care.[1]

Advantages to HFNC

More Reliable Oxygen Delivery

Compared to standard nasal cannula (NC) and other high flow oxygen systems (e.g. Venturi mask), HFNC can better meet the inspiratory demands of patients with respiratory distress and respiratory failure.[1,2] HFNC is able to deliver the set fraction of inspired oxygen (FiO2) more reliably than other oxygen delivery devices by reducing the entrainment of room air and preventing the dilution of oxygen therapy.[3,4] Patients who are in respiratory distress often have high inspiratory flow demands that exceed the flow rates provided by traditional oxygen delivery devices. HFNC thereby improves oxygen delivery by better matching the inspiratory flow demands when patients are in distress.

HFNC is Comfortable and Well Tolerated

HFNC is a well-tolerated form of respiratory support. When compared to other respiratory support devices such as NC, face masks, or interfaces used for non-invasive mechanical ventilation (NIV), HFNC is consistently well tolerated and has higher comfort scores.[4-6] As a component of comfort, improvement in patient's subjective dyspnea improves when HFNC replaces standard oxygen therapy.[5,7,8] In one study, the improvement

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in dyspnea was noted within the first 5 minutes of therapy.[7] When reliable use of the prescribed oxygen delivery device is of consequence, HFNC can provide quick relief and be tolerated for long periods of time.

HFNC Can Reduce Dead Space and Increase End Expiratory Lung Volumes

The physiologic effects of HFNC form the basis for which improvements in clinical outcomes may be explained. High flow rates that can reach, and sometimes exceed, 60 liters per minute (LPM) are able to induce a washout of the nasopharyngeal dead space and allow for enhanced conduction of alveolar gases. A study in healthy volunteers and nasally breathing tracheotomized patients demonstrated clearance of dead space from the nasal cavities, posterior oropharynx, and proximal trachea as flow rates were titrated from 15 LPM to 45 LPM.[9] This is postulated to reduce rebreathing of CO_2 and improve the efficiency of ventilation. There has been much interest in the use of HFNC to provide positive pressure respiratory support. The positive pressure delivered by HFNC is variable during the respiratory cycle and reaches peak pressures on the order of 5 cm H_2O in early expiration.[10] Open mouth breathing can negate the positive pressures measured in the posterior oropharynx. Despite these limitations of open mouth breathing and variable pressure during the respiratory cycle, application of high flow rates increases end-expiratory lung volume (EELV) on electrical impedance tomography.[11,12] Since EELV is equivalent to the functional residual capacity of the lung in the setting of positive pressure, this suggests there is alveolar recruitment and reduction of atelectasis due to some element of positive airway pressure. Improving the efficiency of breathing and improving the end-expiratory lung volume form the basis for the clinical benefits of HFNC.

HFNC Improves Compliance and Work of Breathing in Patients with Respiratory Failure

Early clinical research with HFNC focused on comfort, positive pressure measurements, and oxygen delivery, but precise understanding of physiologic mechanisms remained elusive. More contemporary investigations have studied the impact of HFNC on classic physiologic parameters of the respiratory system. Patients presenting with hypoxic respiratory failure with an average PaO_2: FiO_2 ratio of 135, approximately half of whom had bilateral airspace disease, were studied to determine the impact of HFNC on the pressure-time product (PTP) of the respiratory system, minute ventilation, and dynamic compliance—among other physiologic variables.[13] Compared with physiology parameters obtained while on face mask oxygen, patients demonstrated decreased work of breathing measured by the PTP and respiratory rate, decreased inspiratory effort measured by esophageal manometry and increased dynamic respiratory system compliance after receiving HFNC at 40 LPM for 20 minutes. Further investigation demonstrated improvement with increasing flow rates. In a similar group of patients with hypoxemic respiratory failure (n = 17), increasing flow rates from 30 to 60 LPM progressively decreased inspiratory effort, work of breathing and improved dynamic compliance.[14] Many of the clinical benefits of HFNC may be attributed to improvements in these physiologic parameters.

Clinical Use of HFNC in Hypoxemic Respiratory Failure

HFNC has been shown to be efficacious in improving several clinical end points such as oxygenation, work of breathing, respiratory rate (RR) and dyspnea scores in patients with hypoxemic respiratory failure.[15,16] Despite these benefits, the clinical efficacy of HFNC in large clinical trials has been mixed. A large randomized trial in patients with hypoxic respiratory failure demonstrated mortality improvement with the use of HFNC compared with standard oxygen and NIV, despite not finding improvement in the primary outcome of intubation rate.[17] Subsequent trials and analyses have not consistently demonstrated a mortality benefit in hypoxemic respiratory failure or for the reduction in need for MV.[18,19] Nevertheless, HFNC is a widely used modality and intermediary between NC and tracheal intubation.

HFNC Use in Current SARS-CoV-2 Pandemic

There are currently no prospective clinical trials performed and few reports published regarding the safety or efficacy of use of HFNC in viral pneumonia caused by SARS-CoV-2. In one small retrospective study, the characteristics of 17 patients with severe respiratory failure from SARS-CoV-2 initially treated with HFNC were described.[20] In this cohort, HFNC flow and FiO_2 were adjusted to maintain oxygen saturation (SpO_2) above 93% and failure was defined only as need for NIV or MV. HFNC failure occurred in 41% (n = 7) of these patients and all had PaO_2: FiO_2 ratio <200; 5 of these patients were salvaged with NIV and 2 were intubated. Of those with HFNC success (n = 10), all were noted to have PaO_2: FiO_2 ratio >200, suggesting this may be a discriminative marker. Patients with HFNC success had reported decreases in respiratory rate compared to baseline within 1 hour of initiation (mean 23 vs 26/min $p = 0.03$) but the difference was small and of minimal clinical significance.

Other reports offer anecdotal experience only. In an observational study of a cohort of 52 critically ill patients in Wuhan, China, clinical characteristics and treatment modalities were described.[21] In total, 63.5% of patients were treated with HFNC. Of those surviving (n = 20), 85% (n = 17) were treated with HFNC and 15% (n = 3) with invasive mechanical ventilation. Compared to non-survivors (n = 32), 50% (n = 16) were reported treated with HFNC and 59% (n = 19) were treated with MV. The higher percentage of HFNC use in survivors likely reflects a difference in disease severity, but no clinical endpoints were described in the decision to use or escalate therapy from HFNC to mechanical ventilation. In a retrospective description of 24 critically ill patients in Washington State,

42% (n = 10) were treated with HFNC, and ultimately 18 of the 24 patients required MV.[22] In 59 patients with SARS-CoV-2 related respiratory failure treated with compassionate use remdesivir, at baseline 9% (n = 5) were treated with HFNC.[23] As in the study from Wuhan, specifics of its use were not described, but it does appear to be used as a primary modality in some patients.

In other viral pandemics such as 2009 Influenza A (H1N1) or Middle East Respiratory Syndrome Coronavirus (MERS-CoV) there also are few reports published on the experience or use of HFNC. In a small post hoc analysis of 25 patients admitted for respiratory failure from H1N1 influenza pneumonia, the use of HFNC was evaluated for alleviation of need for mechanical ventilation.[24] All patients were placed on droplet precautions and clear criteria for intubation were established. Of those treated with HFNC therapy on admission (n = 20), 9 (45%) patients successfully avoided mechanical intubation. It was notable that in these patients they had moderate ARDS with median (interquartile range) PaO_2: FiO_2 135 (84-210).

Concerns with HFNC Use

Aerosolization and Spread of Virus Particles with Clinical use

There has been significant concern that use of HFNC in the setting of SARS-CoV-2 may promote the aerosolization and spread of virus particles, possibly placing health care workers (HCW) at risk of contracting the infection. There are no studies published to date to specifically to answer this question. However, a retrospective study investigating risk factors for SARS-CoV-1 transmission to HCW during the 2003 outbreak in Toronto suggests HFNC use was not a significant contributor.[25] In this study, 26/624 HCW caring for patients with SARS-CoV-1 contracted SARS. The highest risk factors (compared to those HCW not contracting SARS) identified were: procedures exposing HCW to the patient's airway; eye or mucus membrane exposure to bodily fluids; intubation of patients; manipulation of oxygen mask or sputum collection. Of patient care procedures described, HFNC was not shown to have increased risk of exposure to respiratory secretions (8% vs 18% p = 0.29). Non-invasive ventilation however was shown to increase risk of respiratory secretions (38% vs 17% p < 0.01) and transmission of SARS. It should be noted that those HCW at higher risk were those with less infection control training, less likely to wear proper personal protective equipment (PPE) in the patient room and wore less effective respiratory protection. Of the HCW that contracted SARS (n = 26), none were reported to be wearing an N-95 or equivalent respiratory protection. Another study evaluating aerosol generating procedures and risk of transmission of SARS to HCW found that the highest risk procedures included: tracheal intubation, non-invasive mechanical ventilation, tracheostomy and bag valve ventilation prior to intubation.[26] They also found HFNC was not associated with risk of aerosolization but only included the previous study described in their analysis.

Experimental Evidence Suggests that HFNC does not Significantly Aerosolize Viral Particles

Experimental evidence suggests also that HFNC does not significantly aerosolize viral particles. Using a patient simulator with variable lung compliance and ability to exhale a smoke mixture visualized with a laser, exhaled air dispersion was studied comparing conventional NC, HFNC and CPAP.[27] Of note, all patients were studied in a negative pressure room with 16 air changes per hour. They found that using HFNC in mild to severe lung disease at 60 LPM resulted in a measured dispersion distance of 7.2 ($\pm$1.8) to 4.8 ($\pm$1.6) cm from the patient's mouth. This increased to 17.2 ($\pm$3.3) cm under normal lung compliance conditions. Compared to conventional NC under similar conditions there was an exhalation distance (sagittal plane to end of the bed) of 60 to 100 cm with flow increasing from 1 to 5 LPM. The authors postulated that the higher dispersion from NC is related to a poor fit in the nostril compared to HFNC, and the lack of humidification forms smaller droplets with larger trajectories. It was however noted that with HFNC, if there was not a tight connection between the cannula to the interface tubing there was a greater dispersion distance of air (62 cm). Whereas the prior study investigated dispersion with typical breathing patterns, another study investigated the impact of cough on the distance of droplet dispersion in healthy volunteers (n = 5) using HFNC at 60 LPM of flow.[28] In this investigation subjects gargled with 10 cc of a colored solution and after a forceful cough the droplet dispersion distance was measured. Compared to distance without HFNC the mean distance (SD) was 2.91 m (1.09) vs 2.48 m (1.03).

The addition of a facemask over the nasal cannula may also further limit particle aerosolization. The performance of a facemask and prevention of aerosol infectivity in exhaled breath samples from patients with viral infections (without supplemental oxygen) has been previously studied. In a prospective study of 37 volunteers with confirmed influenza infection, exhaled particles (during cough) were collected with and without a facemask to evaluate for virus aerosol shedding in coarse (>5 μm) and fine (<5 μm) particles.[29] The use of a mask resulted in a 25 fold reduction in exhaled virus number in coarse particles (95% CI 3.5-180, p = 0.002) and 2.8 fold decrease in fine particles (95% CI 1.5 to 5.2, p = 0.001). Overall, mask use caused a 3.4 fold decrease (95% CI 1.8-6.3) compared to no mask. It was noted that fine particles contained 8.8 fold (95% CI 4.1 to 19) more virus than coarse and could be cultured in 2 individuals. In another study, the efficacy of facemasks (compared to no mask) on viral shedding in exhaled breath was evaluated in 111 patients with confirmed infection with either seasonal coronavirus, influenza or rhinovirus.[30] For coronavirus specifically (n = 17 patients), viral RNA was detected in 30% of droplet particles (>5 μm) and 40% of aerosolized particles (<5 μm) without a facemask. With the use of a facemask there was no virus detected in aerosolized particles (p = 0.02) or droplet particles, however this did not reach statistical significance (p = 0.07). These studies suggest that the use of facemasks in patients infected with

SARS-CoV-2 may significantly reduce viral dispersion to HCW caring for them.

Delayed Tracheal Intubation and Mechanical Ventilation

Delays in escalating medical therapy for patients with impending respiratory failure have created concern that initiating HFNC in patients with hypoxemia may lead to worse outcomes. A study on the use of rescue NIV after extubation failure demonstrated decreased survival compared to those randomized to standard therapy despite similar rates of re-intubation, leading many to conclude that prolonging the time to re-intubation resulted in harm.[31] The adoption of HFNC as a primary or rescue therapy for respiratory failure has led to similar concerns. This was evaluated in a retrospective propensity matched observational trial of 175 patients with respiratory failure that required intubation after failing treatment with HFNC.[32] In those patients with early HFNC failure who were intubated <48 h after initiation ($n = 130$), there was a statistically significant difference in overall mortality compared to those failing >48 h after initiation ($n = 45$), (51 (39.2%) vs 30 (66.7%) $p = 0.001$). Although this latter study has significant limitations, it reinforces that patients at risk of failing HFNC should be vigilantly monitored and intubation should not be delayed for severe respiratory failure.

Using objective criteria while observing patients on HFNC can improve the detection of clinical failure and avoid delays in escalating therapy. An index including SpO_2, FiO_2, and respiratory rate (RR) has been proposed to predict the success and failure of patients placed on HFNC as their disease progresses. A retrospective cohort of patients with pneumonia and hypoxemic respiratory failure was used for the derivation of the ROX (Respiratory rate-OXygenation) index (ratio of SpO_2/FiO_2 to RR).[33] This was followed by a prospective validation study in 191 patients with pneumonia and hypoxemia treated with HFNC. The validation found that values greater than 4.88 were associated with a lower risk of intubation at 2, 6, and 12 hours after the initiation of therapy. ROX values less than 2.85 at 2 hours, less than 3.47 at 6 hours, and less than 3.85 at 12 hours were predictors of HFNC failure.[34] The application of this index may be used to appropriately decide whether to continue or escalate therapy for individual patients and could mitigate any concerns about delays in intubation with the use of HFNC.

Excessive Respiratory Drive in the Setting of Lung Injury May Lead to Patient-Self-Inflicted Lung Injury

A cornerstone of supportive therapy in patents with ARDS has been low tidal volume lung protective ventilation, which has improved outcomes presumably through reduction of ventilator induced lung injury (VILI).[35] In spontaneously breathing patients with lung injury and impaired gas exchange; increased respiratory drive with large tidal volumes has been postulated to exacerbate lung injury in an analogous manner, termed patient-self-inflicted-lung injury (P-SILI).[36] The pathophysiologic basis has been theorized to be the result of large fluctuations of transpulmonary pressure (P_L) leading to delivery of large tidal volumes and overdistention of the smaller aerated and larger dependent atelectatic lung compartments.[37] Brisk diaphragm contraction may lead to intense local variations in P_L predominantly affecting dependent lung, leading to additional stress with the drawing in of gas in from other non-dependent regions (pendelluft phenomenon) and compression with exhalation (atelectrauma).[38] Additionally, pulmonary capillary vascular pressure and blood flow is augmented from large deflections of P_L favoring the formation of pulmonary edema in injured lung units.[39] The harms of dysregulated high respiratory drive thus may lead to a cycle of continued lung injury, respiratory failure and possibly worse outcomes; potentially mitigated by early intubation. Although intriguing and plausible, there is currently no prospective trial that offers conclusive evidence to this theory. Precise clinical measures defining P-SILI are also not established, but it still remains an important clinical construct. Despite the aforementioned benefits of HFNC therapy, it is uncertain whether its application in patients at risk for P-SILI is helpful or harmful.

In an experimental model with spontaneously breathing animals, P-SILI was abrogated with the application of high PEEP; which led to recruitment of dependent lung regions, reduction of large P_L changes and decreased inflammation seen on positron emission tomography.[40] HFNC has been shown to create maximal expiratory nasopharyngeal pressures of 5 cm H20 at 50 LPM flow rates, but are unlikely to be sufficient to recruit dependent lung regions.[10] Despite this limitation, in a small randomized cross-over study the respiratory mechanics of HFNC at various flow rates were compared to facemask in patients with hypoxemic respiratory failure.[14] A flow rate of 60 LPM was shown to significantly decrease changes in transesophageal pressure and esophageal PTP reflecting patient effort and work of breathing. This would suggest that in some patients HFNC may be adequate therapy to remit the risk of P-SILI. Clinical measurements of work of breathing or respiratory drive including use of esophageal balloon manometry are cumbersome and impractical in spontaneously breathing patients with lung injury. Without clear guidance or endpoints, a decision to initiate or continue HFNC therapy to prevent lung injury rests on clinical judgment and gestalt. The incorporation of clinical scores predicting failure of HFNC may also be useful to discriminate in this setting.[34]

Use of HFNC Combined with Prone Positioning

Prone positioning has been investigated and found to improve oxygenation and outcomes in patients with ARDS. Since the PROSEVA trial in 2013, prone positioning has been touted as an effective therapy for the treatment of patients with ARDS.[41] This study included patients with moderate to severe ARDS (PaO_2: $FiO_2 < 150$) and demonstrated a mortality benefit when they received prone positioning for greater than 16 hours per day compared with a control group that was in the supine

position. There is emerging literature on the use of prone positioning in non-intubated patients, especially patients on HFNC therapy. A study of healthy volunteers found an increase in EELV with the use of HFNC at 40 LPM in both the supine and prone positions.[12] While in the prone position, subjects had an improved homogeneity of increase in EELV; HFNC increased the EELV in the ventral lung regions more than dorsal ones in the supine position, whereas HFNC increased both ventral and dorsal lung EELV equally in the prone position.

The use of prone positioning in non-intubated patients with ARDS has been investigated in several small trials and case series. In a small trial of 20 patients with moderate ARDS due to influenza pneumonia, patients with HFNC therapy and prone positioning for an average duration of 2 hours showed an increase in PaO_2: FiO_2 and avoidance of intubation in 55% of patients ($n = 11$).[42] In a case series of 6 patients with moderate ARDS of non-infectious etiology, therapy with HFNC plus prone positioning was successful in stabilization and intubation was avoided in 4 patients.[43] Both these studies are limited due to small size and there was overlap with NIV therapy in both. In ARDS due to SARS-CoV-2, several published case reports have documented success using HFNC with prone positioning in improving oxygenation and avoiding intubation in those patients.[44,45]

In a recent large feasibility study of 47 non-intubated patients with moderate ARDS from SARS-CoV-2 the benefits of prone positioning in non-intubated patients (without HFNC) was studied.[46] Using oxygen support with helmet CPAP or supplemental oxygen (Venturi system or reservoir bag) patients were proned for a minimum of 3 hours with blood gas analysis done at baseline, 10 minutes after being proned and again 1 hour after supination. On average there was a 50% increase in PaO_2: FiO_2 ratio once prone (285.5 mmHg vs 180.5 mmHg, $p < 0.0001$); however the improvements in PO_2 (compared to baseline) were lost or were not statistically significant once supine position was resumed. In evaluation of the comfort of the therapy the majority rated it as good or excellent, none rated it unacceptable. Overall, these reports are clearly limited and have not shown a convincing outcome benefit compared to those that are intubated. Regardless, HFNC with prone positioning appears to be a safe and reasonable intervention to attempt in cooperative patients to improve oxygenation indices and may possibly delay or avoid the need for intubation.

Rationale for use of HFNC in SARS-CoV-2

The optimal initial strategy of respiratory support in patients with SARS-CoV-2 pneumonia is uncertain. Published retrospective cohort studies have reported that the majority of critically ill patients with SARS-CoV-2 ultimately require endotracheal intubation and mechanical ventilation.[47,48] However, there may be select patients with less severe disease in which HFNC may be an adequate initial therapy; but factors identifying these patients have yet to be defined. The debate as to whether it is a useful therapy despite lacking strong supportive evidence has been illustrated in several opinion pieces dismissing a complete prohibition.[49,50] In our regional hospitals, which include academic tertiary referral and other community hospital centers, intensivists have a mixed approach in their initial management of these patients (personal communications). In some centers, these patients are exclusively managed with early intubation due to many of the concerns with HFNC addressed earlier above; while others have allowed some patients initial trials of non-invasive ventilatory support (i.e. HFNC, CPAP or BiPAP). The former strategy may be efficacious, but in the setting of a pandemic comes at the cost of significant resource utilization (e.g. ventilator availability, nursing and respiratory support). In our experience, many of these patients also require high doses of sedatives to maintain ventilator synchrony that contribute to drug shortages as well as complications such as delirium, prolonged intubation and ventilator associated pneumonia. In a pandemic scenario, identification of patients with less severe disease who can be stabilized with HFNC or avoid intubation and allow allocation of resources to those more critically ill clearly has benefits. There are other clinical scenarios where HFNC may also be useful. For example, in the management of oxygen support post-extubation or in those that have chosen a do not intubate code status and need respiratory support. To our knowledge these both have not been studied in the SARS-CoV-2 population.

Currently there is little data available to promote or refute the use of HFNC in SARS-CoV-2. Published experience appears limited and use is guided by international and national guidelines, expert opinion and institutional culture. The studies mentioned above do not definitively show evidence that HFNC in SARS-CoV-2 or other viral pneumonia is efficacious nor completely safe for HCW treating them. The addition of prone positioning may improve the success of HFNC therapy but the studies supporting this practice are limited with mixed results. There appears to be no supplemental oxygen treatment that is completely safe to HCW in terms of aerosolization risk. Any patient suspected or confirmed with SARS-CoV-2 is at extremely high risk of aerosolizing viral particles with a cough or sneeze even without oxygen therapy. Retrospective evidence from SARS-CoV-1 studies and experimental evidence suggest that HFNC was not a significant risk factor for HCW developing SARS and does not significantly disperse exhaled air droplets. The use of a surgical facemask over the patients face and cannula may significantly reduce aerosolization and dispersal of viral particles. For HFNC in particular, the pooling of condensation in the circuit limb may also be a significant source of viral contamination. Alteration of ambient room temperature above 20°C has been shown to decrease condensation.[51]

Patients with respiratory failure due to infection with SARS-CoV-2 who receive HFNC therapy should be placed in negative pressure rooms (defined as 12 air changes per hour) or a room with natural ventilation (defined as flow of 160 L/sec) if a negative pressure room is unavailable, as recommended by the World Health Organization.[52] This underscores the importance of proper education and use of PPE by HCW caring for these

Table 1. Society and Organization Guidelines for the Use of HFNC in SARS-CoV-2.

Organization	Recommendation	Statement
World Health Organization (WHO)[52]	Caution	• HFNC should only be used in selected patients with hypoxemic respiratory failure. • Patients treated with either HFNC or NIV should be closely monitored for clinical deterioration.
Society of Critical Care Medicine (SCCM)[53]	Use	• For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we suggest using HFNC over conventional oxygen therapy (weak recommendation, low quality evidence). • In adults with COVID-19 and acute hypoxemic respiratory failure, we suggest using HFNC over NIPPV (weak recommendation, low quality evidence). • In adults with COVID-19 receiving NIPPV or HFNC, we recommend close monitoring for worsening of respiratory status, and early intubation in a controlled setting if worsening occurs (best practice statement).
Italian Thoracic Society (AIPO-ITS)[54]	Use	• When available, use a high-flow oxygen blender of at least 70 L/min • Increase FiO2 up to 0.9 -1 to guarantee just enough oxygenation • High oxygen flows (HFO) are possible as a window between low oxygen and CPAP or in the absence of CPAP/NIV or as a therapeutic ceiling option (HFO presents higher FiO2 possibility but there is hypothetically a greater risk of drops diffusion and low PEEP levels are generated)
Australia and New Zealand Intensive Care Society (ANZICS)[55]	Use	• We therefore recommend that airborne PPE precautions should be used to care for all COVID-19 patients in intensive care. This includes the use of high flow nasal oxygen in non-ICU environments. • HFNC is a recommended therapy for hypoxia associated with COVID-19 disease, as long as staff are wearing optimal airborne PPE. • The risk of airborne transmission to staff is low with well fitted newer HFNC systems when optimal PPE and other infection control precautions are being used. Negative pressure rooms are preferable for patients receiving HFNC therapy.
American Association for Respiratory Care (AARC)[56]	Use	• In patients with early hypoxemia, consider high flow nasal oxygen. This is controversial, with some concerns regarding environmental contamination. If used, there should be a low threshold for failure and urgent intubation. Some clinicians will elect to avoid high flow nasal cannula. • Environmental controls should be considered with an emphasis on caregiver protection.
National Institutes of Health (NIH)[57]	Use	• For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula oxygen over noninvasive positive pressure ventilation

patients for safe practice. Multiple organizations and professional societies have made recommendations (based on available data and extrapolations) for use of HFNC in SARS-CoV-2 (Table 1).

Summary Regarding Use of HFNC in SARS-CoV-2

Patients in whom HFNC is considered should be chosen carefully. In those meeting criteria for more severe disease or who are in significant respiratory distress, early intubation should be performed. Patients considered for HFNC therapy should have proper isolation, ideally placed in negative pressure rooms with their faces and cannulas covered with a surgical mask. HCW should be donned in proper PPE attire with airborne precautions. In our experience, generally we allow for a short trial of HFNC in patients with hypoxemia from SARS-CoV-2 pneumonia that are awake, protecting their airway, controlling secretions and are not in obvious respiratory distress. Patients should be monitored closely for improvements in SpO_2 or PaO_2. Depending on clinical scenario and degree of patient illness and cooperation, a trial of prone positioning may also be attempted. Decisions to continue HFNC treatment would depend on clinical progression, serial lab measures and clinical stability. The ROX index (<2.85 at 2 hours or less) may be a useful discriminator of patients that are in early danger of failing HFNC, but the index has not been studied specifically in this population of SARS-CoV-2. In contrast, we preferentially intubate early those patients that have altered mental status, shock, uncontrolled acidosis, hypercapnia or severe hypoxemia and those in significant respiratory distress.

Authors' Note

D.A.S. and M.G.A. contributed to the research, writing and editing of this manuscript.

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