Proposed Management of COVID-19 with High-Flow Nasal Cannula

Version 4 – April 15, 2020

This document collates society & institutional guidelines and offers guidance for use of HFNC for treatment of COVID-19 disease while minimizing risk to staff. This is an evolving area without definitive evidence or uniform policy that underwent multi-disciplinary discussion.

**Recommendation**

HFNC may have a role in the subset of COVID-19 patients who have essentially normal compliance but severe symptomatic hypoxemia.

**Oxygen Goals in COVID-19**

- Medical Team should discuss & agree on oxygen goals that balance the risk of ventilator-induced lung injury vs. benefits of increased oxygen delivery.
- Considerations include:
  - Use resting SpO$_2$ over several measurements; any exertion causes dramatic hypoxemia.
  - Leave some margin of safety, i.e. FIO$_2$ ≤0.8, so can increase if intubating the patient.
- SpO$_2$ 80-85% without symptoms **may** be acceptable, 85-90% w/ dyspnea or evidence of minor tissue hypoxia **may** be acceptable.

**Indications for Use**

- Patients with inadequate response to 15L NRB mask O$_2$ challenge (SpO$_2$ <85%)
- Patients with asymptomatic hypoxemia & evidence of end organ or tissue hypoxia
- Do not use for air hunger in patients on comfort care.

**Infection Control Safety**

- Airborne + droplet + contact precautions
- Negative pressure room or ward
- Should not be routinely deployed in ED or acute care units unless limited ICU capacity
- Turn off HFNC for patient movement through the hospital

**Safety**

- Any flow is acceptable if care team wearing airborne PPE (see Flow section below).
- Keep HFNC off until patient has simple surgical facemask in place over HFNC & RT is away from face. (Ideally > 2m / 6 ft.).
- Turn off HFNC for any removal, adjustment, or transport.
- Correct size with snug fit of interface

**Evaluation of Effectiveness**

- HFNC FIO$_2$ >0.8 at rest to keep SpO$_2$ ≥85% for 4 hours continuous: consider intubation
- Use ROXI (see below) or work of breathing (RR > 40 as surrogate) or resting SpO$_2$ to predict failure. Re-assess 2 hours after initiation:
  - If SpO$_2$ ≥85% + RR<40 + ROXI >3.85, continue HFNC
  - If SpO$_2$ ≥85% + RR<40 + ROXI 2.85-3.85, continue HFNC 6 hours & re-assess
  - If SpO$_2$ <85% or RR≥40 or ROXI <2.85, consider intubation

Ver 4, April 15, 2020
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## Summary of Guidelines & Recommendations of HFNC in COVID-19

<table>
<thead>
<tr>
<th>Society or Institution</th>
<th>Use?</th>
<th>Recommendation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO</td>
<td>Yes</td>
<td>HFNC … systems with good interface fitting [i.e., good seal, no air leak] do not create widespread dispersion of exhaled air and therefore should be associated with low risk of airborne transmission.</td>
<td>Raboud 2010. HF O2 not associated w/ HCW transmissio n</td>
</tr>
<tr>
<td>Surviving Sepsis Campaign</td>
<td>Yes</td>
<td>For adults with … acute hypoxemic respiratory failure despite conventional oxygen tx, we suggest using HFNC over conventional oxygen therapy (weak recommendation, low quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Society Critical Care Medicine</td>
<td>Maybe</td>
<td>Practices such as … high-flow nasal cannula (HFNC) … may veer away from everyday standards.</td>
<td></td>
</tr>
<tr>
<td>Australia New Zealand Intensive Care Society</td>
<td>Yes</td>
<td>High Flow Nasal Oxygen (HFNO) is a recommended therapy for hypoxia associated with COVID-19 disease, as long as staff are wearing optimal airborne PPE. We suggest avoidance of HFNO use to preoxygenate patients prior to intubation.</td>
<td></td>
</tr>
<tr>
<td>University College London Hospitals</td>
<td>Maybe</td>
<td>Consider HFNO in pts. who SpO\textsubscript{2} ≥95% (&gt;90% COPD) w/ 15L NRB “O\textsubscript{2} Challenge” (CPAP for pts. w/ worse oxygenation.)</td>
<td></td>
</tr>
<tr>
<td>Wuhan University</td>
<td>Yes</td>
<td>Use in pts. with P/F 200-300 @ FiO\textsubscript{2} 1.0 for 2h. Use ROX index to evaluate continued use: (SpO\textsubscript{2}≥93% + RR&lt;25 + ROXI&gt;3.85) continue HFNO (SpO\textsubscript{2}≥93% + RR 25-30 + ROXI 2.85-3.85) HFNO x6h (SpO\textsubscript{2}&lt;93% or RR≥30 + ROXI&lt;2.85) stop HFNO</td>
<td></td>
</tr>
<tr>
<td>Shanghai Medical Association</td>
<td>Yes</td>
<td>If 1-2h nasal or mask oxygen treatment does not meet the treatment requirements, no improvement in respiratory distress, or during treatment hypoxemia and/or respiratory distress, or oxygenation index of 150 to 200 mmHg, use HFNO.</td>
<td></td>
</tr>
<tr>
<td>Italian Society Infectious Disease</td>
<td>Yes</td>
<td>Suggest use if &gt;2 of: - Staccato speech (can’t count to 20 quickly after deep breath) - RR &gt; 22 - PaO\textsubscript{2}&lt;65mmHg or SpO\textsubscript{2}&lt;90% - Significant worsening of CXR</td>
<td></td>
</tr>
<tr>
<td>Brigham &amp; Women’s Hospital</td>
<td>No</td>
<td>Avoid high-flow nasal cannula (HFNC) … for ARDS.</td>
<td></td>
</tr>
<tr>
<td>Intermountain Health System</td>
<td>No</td>
<td>Proceed with intubation — no NIPPV/HFNC — if requiring therapy &gt;6L via nasal canula given (1) NIPPV/HFNC likely does not prevent intubation; (2) initial NIPPV/HFNC may yield worse outcomes; and (3) increased droplet production increasing risk to HCW.</td>
<td></td>
</tr>
<tr>
<td>NewYork-Presbyterian</td>
<td>Yes</td>
<td>“When using HFNC, use minimal flow necessary to maintain SpO\textsubscript{2} &gt; 88% - 94%; lower flow rates for example under 30 L/min may have less aerosolization. In attempt to minimize flow, titrate FiO\textsubscript{2} to maximum support prior to increasing flow greater than 30 L/min. ”</td>
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Proposed Management of COVID-19 with High-Flow Nasal Cannula

**Ideal Flow**
Ideal flow is unknown. Higher flows may better match high inspiratory flow by the patient, thus causing FIO₂ to be closer to the FDO₂ by limiting entrained air. Higher flows also may provide minimal Peep (as reflected by slightly higher end-expiratory lung volume), and may reduce anatomic dead space. Studies below used 40-60 LPM flow. Higher flows appear to improve oxygenation and reduce respiratory rate and may be associated with improved outcomes in one RCT.

**Advantage of Higher Flow**
- Improved FIO₂ delivery
- Reduced Work of Breathing
- Minor increase in Peep

**Risk of Higher Flow**
- Increase in droplet spread distance by 4cm (2in) at rest, 40cm (15in) w/ cough
- Delay in intubation

**Messika 2015**: Observational, single-center study of 560 patients with ARDS; 180 received noninvasive support, HFNC (60 LPM) in 51 patients (29%). The intubation rate in these subjects was 40%. Higher SAPS II & additional organ failure were associated with HFNC failure. There was a trend of lower PaO₂/FIO₂ and higher respiratory rate in patients who failed HFNC.

**Frat 2015**: FLORALI study. RCT of 310 patients with acute hypoxemic respiratory failure (P/F ≤ 300) treated with HFNC (50 LPM) for ≥2 days, standard oxygen therapy via face mask, or NIPPV. The intubation rate was 38% in the high-flow–oxygen group, 47% in the standard group, and 50% in the noninvasive-ventilation group. The hazard ratio for death at 90 days was 2.01 with standard oxygen versus high-flow oxygen & 2.50 with noninvasive ventilation versus high-flow oxygen.

**Jones 2016**: HOT-ER Study. Pragmatic open RCT in adult subjects with hypoxia and tachypnea presenting to a tertiary academic hospital ED. 303 patients randomized to HFNC (40 LPM) or standard O₂. Intubation in the ED occurred in 3.6% of the HFNC group and 7.2% of the standard oxygen group. 5.5% in HFNC versus 11.6% in the standard O₂ group required mechanical ventilation within 24 h. There was no difference in mortality or stay. No significant difference in any of the findings.

**Mauri 2017**: Prospective randomized crossover study of 15 patients in acute hypoxemic respiratory failure (P/F ≤300). HFNC (40 LPM) or standard non-occlusive facial mask at 12L/min. HFNC significantly improved PaO₂ and lowered respiratory rate.

**Mauri 2017**: Prospective randomized crossover study of 17 patients in acute hypoxemic respiratory failure (P/F ≤300). A standard non-occlusive facial mask and HFNC at different flow rates (30, 45 and 60 LPM) were randomly applied, while maintaining constant FiO₂. At increasing flow rate, HFNC reduced ΔPes & Ptp and improved end-expiratory lung volume, and oxygenation. Higher HFNC flow rate also progressively reduced minute ventilation.
Proposed Management of COVID-19 with High-Flow Nasal Cannula

Azoulay 2018: HIGH RCT enrolled 776 adult immunocompromised patients with acute hypoxemic respiratory failure (PaO2 <60 mmHg or SpO2 <90% on room air, or tachypnea >30/min or labored breathing or respiratory distress, and need for oxygen >6 L/min) to conventional oxygen of HFNC (50 LPM) flow & FIO2 to keep SpO2≥95%. Mortality on day 28 was not significantly different between groups (35.6% vs 36.1%). Intubation rate was not significantly different between groups (38.7% vs 43.8%). Patients randomized to HFNC had a higher P/F (150 vs 119) after 6 hours.

Effectiveness

Evaluation of Effectiveness: Summary

- Re-assess 2 hours after initiation:
  - If SpO2 ≥85% + RR<40 + ROXI >3.85, continue HFNC
  - If SpO2 ≥85% + RR<40 + ROXI 2.85-3.85, continue HFNC 6 hours & re-assess
  - If SpO2 <85% or RR≥40 or ROXI <2.85, consider intubation

- HFNC FIO2 >0.8 at rest to keep SpO2 ≥88% for 4 hours continuous: consider intubation
- RR ≥40 for 4 hours continuous with increased work of breathing may predict failure
- Use ROXI (see below) or work of breathing (RR > 40 as surrogate) or resting SpO2 to predict failure.

Rodriguez 2017: Secondary analysis of prospective study in critically ill subjects admitted to the ICU with ARF due to influenza infection requiring mechanical ventilation. Described course of three groups: (1) subjects who received NIV immediately after ICU admission & then failed, (2) subjects who received NIV immediately after ICU admission & succeeded, (3) subjects who received invasive mechanical ventilation immediately. Of 1,898 subjects, 806 underwent NIV, and 56.8% of them failed. SOFA score >5 had a higher risk of NIV failure (odds ratio 3.3). ICU mortality was higher in subjects with NIV failure (38.4%) compared with invasive mechanical ventilation subjects (31.3%).

Zhou 2020: Observational study 191 pts. from Jinyintan Hospital & Wuhan Pulmonary Hospital. 54 (28%) died in hospital. 41 pts. (21%) received High-flow nasal cannula oxygen therapy. HFNC was used more often in non-survivors (61%) vs. survivors (6%).

Wang 2020: Retrospective review of 318 COVID-19 patients in Chongqing, China. 27 with severe acute respiratory failure. Of 17 HFNC patients, 7 (41%) experienced HFNC failure. HFNC failure rate was 0% in patients with PaO2/FiO2 > 200 mmHg vs. 63% in those with PaO2/FiO2 ≤ 200 mmHg. Compared with baseline, the respiratory rate significantly decreased after 1–2 h of HFNC in successful group, but did not change significantly in the unsuccessful group. P/F ratio > 200 was more common in the HFNC success group, both at initiation and after 2 hours.
Proposed Management of COVID-19 with High-Flow Nasal Cannula

Roca 2019: 2-year multicenter prospective observational cohort study including patients with pneumonia treated with HFNC. 36% of the patients went on to intubation & mechanical ventilation. Cox proportional hazards modeling of ROX association with HFNC outcome. Among the 191 patients treated with HFNC in the validation cohort, 68 (35.6%) required intubation. The prediction accuracy of the ROX index increased over time (area under the receiver operating characteristic curve: 2 h, 0.679; 6 h, 0.703; 12 h, 0.759). ROX greater than or equal to 4.88 measured at 2 (hazard ratio, 0.434; 95% confidence interval, 0.264–0.715; P = 0.001), 6 (hazard ratio, 0.304; 95% confidence interval, 0.182–0.509; P , 0.001), or 12 hours (hazard ratio, 0.291; 95% confidence interval, 0.161–0.524; P, 0.001) after HFNC initiation was consistently associated with a lower risk for intubation. A ROX less than 2.85, less than 3.47, and less than 3.85 at 2, 6, and 12 hours of HFNC initiation, respectively, were predictors of HFNC failure. Patients who failed presented a lower increase in the values of the ROX index over the 12 hours. Among components of the index, oxygen saturation as measured by pulse oximetry/FIO2 had a greater weight than respiratory rate.

<table>
<thead>
<tr>
<th>Hours After HFNC Initiation</th>
<th>Lower Risk Intubation</th>
<th>Predictor of HFNC Failure</th>
</tr>
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<tbody>
<tr>
<td>2 hours</td>
<td>ROXI &gt; 4.88</td>
<td>ROXI &lt; 2.85</td>
</tr>
<tr>
<td>6 hours</td>
<td>(at all time points)</td>
<td>ROXI &lt; 3.47</td>
</tr>
<tr>
<td>12 hours</td>
<td></td>
<td>ROXI &lt; 3.85</td>
</tr>
</tbody>
</table>

Example 1: SpO2 90% on FIO2 0.5, RR 32, 12h after initiation
ROXI = (90/0.5)/32 = 5.63
lower risk intubation

Example 2: SpO2 90% on FIO2 0.8, RR 32, 12h after initiation
ROXI = (90/0.8)/32 = 3.52
predicts HFNC failure & need for intubation

Safety
High-Flow Nasal Cannula (HFNC) is an aerosol-generating procedure. Increased droplets may be limited to close proximity to the patient.

Cheung 2004: NIV prevented IMV in 70% of patients with SARS; no infection in 155 HCWs. Examined the efficacy of NIV in early ARDS and also evaluated the infection risk among healthcare workers who had direct contact with patients on NIV. A total of 22 patients needed NIV and a total of 155 healthcare workers, including doctors, nurses and healthcare assistants, were exposed to these patients on NIV therapy. Coronavirus serology was obtained in 97% of healthcare workers. NIV equipped with expiratory bacterial and viral filters was provided in isolated cubicles in the ward or ICU,
Proposed Management of COVID-19 with High-Flow Nasal Cannula

which were centrally air-conditioned, and fitted with exhaust ventilation fans to achieve negative pressure flow. This study concluded that NIV was not only effective in preventing IMV in 70% of patients with acute respiratory failure due to SARS but effectively reduced the ICU length of stay or avoided ICU admission. Moreover, no infection was noted in any of the 155 healthcare workers. Their serology tests for coronavirus were negative. The potential risk of particle dispersion and spread of infection due to NIV must not be overlooked, even though, at present, the data remains inconclusive.

**Hui 2019**: HFNC airflow leakage distance 13cm @ 30L flow.
Human patient simulator (HPS) in an isolation room with 16 air changes/hour. CPAP was delivered at 5–20 cmH2O via nasal pillows (Respirronics Nuance Pro Gel or ResMed Swift FX) or an oronasal mask (ResMed Quattro Air). HFNC, humidified to 37°C, was delivered at 10–60 L/min. Exhaled airflow was marked with intrapulmonary smoke for visualization and revealed by laser light-sheet. Normalized exhaled air concentration was estimated from the light scattered by the smoke particles. Significant exposure was defined when there was ≥20% normalized smoke concentration.

In the normal lung condition, mean±SD exhaled air dispersion, along the sagittal plane, increased from 186±34 to 264±27 mm and from 207±11 to 332±34 mm when CPAP was increased from 5 to 20 cmH2O via Respirronics and ResMed nasal pillows, respectively. Leakage from the oronasal mask was negligible. Mean±SD exhaled air distances increased from 65±15, 130±11, 172±33mm when HFNC was increased from 10, 30, 60 L/min. Air leakage to 620 mm occurred laterally when HFNC and the interface tube became loose.

**Kotoda 2019**: Manual repositioning of the cannula significantly increased the water dispersal.
This study aimed to investigate the risk of pathogen dispersal during high-flow nasal therapy. Liquid and bacterial dispersal were assessed via in-vitro experimental set-ups using a manikin. Thickened water or fresh yeast solution mimicked saliva and nasal mucus secretions. In the liquid dispersal experiment, water was detected only on the sheet placed in front of the manikin’s face. Manual repositioning of the cannula significantly increased the water dispersal. Water dispersal was not detected on the sheets placed 5 m away from the manikin. Similar to the liquid dispersal experiment, yeast colony formation was observed only on the dish that was closest to the manikin’s face. Manual repositioning of the cannula significantly increased the colony formation. Dispersal was observed in two dishes placed in front of and lateral to the manikin’s face. Colony formation was not observed on the dishes placed 5 m away from the manikin.

**Leung 2019**: Overall negative study. In a secondary outcome, at six air changes/hr, total bacterial count on plates placed at 1.5 m while the patients were using HFNC was statistically significantly higher than when using an oxygen mask.
This randomized controlled crossover non-inferiority trial evaluated the degree of environmental contamination by viable bacteria associated with the use of high-flow nasal cannula compared with conventional oxygen mask for critically ill patients with Gram-negative pneumonia. The results from 19 patients (of 196 screened) with full data sets are presented. Mean (SD) oxygen flow rate while using O2 mask was 8.6 (2.2) L/min and the FiO2 while using HFNC was 0.5 (0.1). No difference in GN bacteria count between the HFNC and O2 mask use for air samples, settle plates at 0.4 or 1.5 m, and at six or at 12 air changes per hour. At six air changes per hour, the total bacterial count on plates placed at 1.5 m while the patients were using HFNC was statistically significantly higher than when using an
Proposed Management of COVID-19 with High-Flow Nasal Cannula

oxygen mask, after one and two days of incubation. Otherwise, no difference in total bacteria count was detected between HFNC and mask use.

**Zou 2020:** High viral loads detected soon after symptom onset, higher viral loads in nose than throat. Analyzed the viral load in nasal and throat swabs obtained from the 17 symptomatic patients in relation onset of any symptoms. Higher viral loads were detected soon after symptom onset, with higher viral loads detected in the nose than in the throat. Our analysis suggests that the viral nucleic acid shedding pattern of patients infected with SARS-CoV-2 resembles that of patients with influenza and appears different from that seen in patients infected with SARS-CoV.

**Loh 2020:** Measured distance traveled droplets expelled by maximal cough in 5 seated, healthy volunteers. Cough-generated droplets spread to a mean (standard deviation) distance of 2.48m at baseline and 2.91m while wearing a well-fitting HFNC at 60 LPM flow. Maximum cough distance of 4.50m. The distance of droplet dispersion from coughing increased by an average of 0.42m with HFNC.

**Leonard 2020:** **Performed by Vapotherm (HFNC company).** Using computational fluid dynamic (CFD) simulation, modeled HFNC on simulated architecture of a petite adult female, sinusoidal breathing a 500ml tidal volume at 32 breaths per minute and a 1:1 Inspiratory/expiratory. HVNI flow was modeled at 40 LPM through a model of Vapotherm Adult Small/Pediatric cannula. Low Flow Oxygen delivery was modeled using a similar cannula delivering 6 LPM continuous flow. Simulated surgical mask placed on model. See Table 1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>% particles trapped in mask</th>
<th>% particles &lt;1m spread</th>
<th>% particles &gt;1m spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>No oxygen</td>
<td>No Mask</td>
<td>69.0%</td>
<td>31.0%</td>
</tr>
<tr>
<td>No oxygen</td>
<td>Mask</td>
<td>87.2%</td>
<td>7.8%</td>
</tr>
<tr>
<td>40 L/min HFNC</td>
<td>Mask</td>
<td>83.2%</td>
<td>0.9%</td>
</tr>
<tr>
<td>6 L/min NC</td>
<td>Mask</td>
<td>73.6%</td>
<td>19.5%</td>
</tr>
</tbody>
</table>

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