RELIAS MEDIA

Vol. 28, Issue 4, July 2020
ReliasMedia.com

Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

SPECIAL FEATURE

High-Flow Nasal Cannula Oxygen Therapy in Adult Acute Care

By J. Brady Scott, MSc, RRT-ACCS, AE-C, FAARC, FCCP

Associate Professor, Director of Clinical Education, Respiratory Care Program, Rush University, Chicago

Mr. Scott reports that he receives research/grant support from Teleflex, Inc., and serves as a consultant for Ventec Life Systems.

A relatively new modality, high-flow nasal cannula (HFNC) oxygen therapy is used commonly to treat acute respiratory failure. HFNC oxygen therapy enables clinicians to deliver warmed, humidified gas at flow rates that meet or exceed the inspiratory flow demands of the patient.[1,2] For the sake of this article, HFNC will refer to devices that deliver flow rates between 25 L/min and 60 L/min. High-flow cannulas with a flow range of 6 L/min to 15 L/min will not be discussed.

THE INTERFACE

Noninvasive ventilation (NIV) has been studied extensively for acute hypercapnic and hypoxemic respiratory failure. In many studies, NIV has been shown to be quite successful. That said, a known cause of NIV failure is intolerance of the interface. One of the perceived benefits of HFNC oxygen therapy is comfort and tolerability. The cannula interface has been shown to be generally well tolerated, which improves patient compliance with the modality.[3-5] Improved compliance, balanced with an improvement in oxygenation and ventilation, makes HFNC an attractive treatment option.[1]

The cannula interface varies by manufacturer and is a distinguishing characteristic between commercially available devices. The high-velocity nasal insufflation device (Hi-VNI) uses a cannula that has a narrow internal diameter, which produces the higher flow velocity (flow range from 5 L/min to 40 L/min). In contrast, the Airvo 2 system uses a large-bore circuit and cannula interface (flow range from 2 L/min to 60 L/min). At this time, it is not

Financial Disclosure: *Critical Care Alert*'s Physician Editor Betty Tran, MD, MSc, Nurse Planner Jane Guttendorf, DNP, RN, CRNP, ACNP-BC, CCRN, Peer Reviewer William Thompson, MD, Executive Editor Shelly Morrow Mark, Editor Jason Schneider, Accreditations Director Amy M. Johnson, MSN, RN, CPN, and Editorial Group Manager Leslie Coplin report no financial relationships relevant to this field of study.

Critical Care [ALERT]
Authoritative, evidence-based summaries for the critical care clinician

Critical Care Alert (ISSN 1067-9502) is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Critical Care Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

GST Registration Number: R128870672.

SUBSCRIBER INFORMATION
(800) 688-2421
customerservice@reliasmedia.com
ReliasMedia.com

Back issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

ACCREDITATION

Relias LLC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Relias LLC designates this enduring material for a maximum of 2 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Relias LLC is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Contact hours [2] will be awarded to participants who meet the criteria for successful completion. California Board of Registered Nursing, Provider CEP#13791.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 MOC Medical Knowledge points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

This CME activity is intended for critical care physicians and nurses. It is in effect for 36 months from the date of the publication.

clear if either offers an advantage over the other. Clinicians charged with applying HFNC should be familiar with interface sizing options and recommendations to maximize performance and comfort.

PHYSIOLOGIC EFFECTS OF HIGH-FLOW NASAL CANNULA

In addition to comfort, HFNC has important physiologic benefits, including positive airway pressure, adequate heating and humidification of inspired gases, washout of anatomic dead space, and a more stable delivery of fraction of inspired oxygen (FiO_2).

Positive Pressure

An often-cited advantage of HFNC is the ability to generate some degree of positive pressure.[1,6] Although HFNC is an open system, some studies have shown an increase in pharyngeal pressures and end-expiratory lung volumes (EELV).[7-9] The increase in EELV is interesting, since it may reflect an increase in functional residual capacity and, thus, some degree of alveolar recruitment. The increase in alveolar recruitment from the positive pressure generated by HFNC may improve gas exchange. The positive pressure effect of HFNC is complicated by the reality that patients often breathe with their mouths open. Substantial variability in pharyngeal pressures have been demonstrated in studies evaluating the effects of having the mouth closed or open.[1,6-10] Body mass index, lung heterogeneity, and device flow rate also may play a role in the variability of lung recruitment from HFNC.[1,6]

Adequate Heating and Humidification of Inspired Gases

Commercially available HFNC devices are capable of delivering well-conditioned (heated and humidified) gases to patients, as long as HFNC flow is higher than patient inspiratory flow. If device flow is lower than patient inspiratory flow, the patient will inspire drier room air. Properly warmed and humidified gases improve mucociliary function, facilitate secretion clearance, minimize airway constriction, and limit the metabolic cost of breathing.[1,6,11,12]

A 'More Stable' Delivery of FiO_2 by Meeting or Exceeding Inspiratory Demand

When device flow is greater than a patient's peak inspiratory flow, HFNC is capable of delivering a stable FiO_2, since patients mainly breathe in gas delivered by the device. This minimizes room air entrainment that can dilute the delivered FiO_2. Since patients control their own inspiratory flow rate and tidal volume, there may be some variability in the actual FiO_2 delivered to the patient.[13,14]

Washout of Anatomic Dead Space

Carbon dioxide (CO_2) is washed out of the anatomic dead space during HFNC therapy. This creates an efficiency in terms of gas exchange, because a higher fraction of minute volume is involved.[14] According to Delorme et al,[15] this is considered a key mechanism in patients with respiratory failure in terms of reducing respiratory effort and improving comfort.

RECENT EVIDENCE

At least 20 randomized controlled trials (RCTs) and 10 meta-analyses on HFNC for adults have been published in the past two years.[2] Many of these studies have evaluated critical care conditions treated with HFNC, such as acute hypoxemic respiratory failure (AHRF), post-extubation, pre-oxygenation before intubation, and chronic obstructive pulmonary disease (COPD).

For patients with AHRF, several older studies demonstrated that HFNC was superior to conventional oxygen therapy and non-inferior to NIV for clinical improvements in oxygenation and avoidance of intubation. However, a paper published in 2018 on HFNC use in immunocompromised patients showed no differences in intubation and mortality between the HFNC and oxygen therapy groups.[16] Subsequently, Rochwerg et al[17] published a systematic review and meta-analysis in 2019 that showed the rate of intubation was lower in patients treated with HFNC when compared to those treated with conventional oxygen therapy. However, there was no difference in intensive care unit (ICU) length of stay, hospital length of stay, and mortality

between the two groups.[2,17] That review excluded studies that included post-extubation respiratory failure. Also in 2019, Shen et al[18] found that patients with a PaO_2/FiO_2 of > 200 mmHg had the greatest benefit from HFNC. Interestingly, post-extubation patients had a particularly positive benefit from HFNC in their study. In an analysis of studies completed in an emergency department setting, Tinelli et al[19] found no benefit of using HFNC over conventional oxygen therapy in subjects with AHRF.

Regarding the role of HFNC for patients after extubation, Zhu et al[20] published a systematic review and meta-analysis of patients undergoing a planned extubation. They found that HFNC reduced respiratory failure after extubation or risk of re-intubation in some studies. In their study, the authors noted only about one-third of patients in both the HFNC and conventional therapy groups were re-intubated, which may underscore the importance of care escalation from one modality to the other in an attempt to mitigate the need for reintubation.[2] Other RCTs subsequently published demonstrated a benefit of HFNC when compared to conventional oxygen therapy. For post-cardiac surgery patients, HFNC use prophylactically after extubation reduced the need for NIV. HFNC also was shown to decrease hospital length of stay and ICU readmission in this group.[21,22] For postoperative obese patients, HFNC use after extubation demonstrated some benefit regarding oxygenation levels after three hours and a reduction in postoperative pulmonary complications.[23] It is important to interpret these results cautiously, since they are contradictory to other studies with similar populations.[24,25]

For patients deemed high-risk at extubation, the data are a bit unclear regarding whether HFNC is non-inferior to NIV. A paper published in 2016 found no significant differences in re-intubation rates between patients with risk factors for extubation failure who were treated with HFNC or NIV. The authors did note a higher incidence of post-extubation failure in the NIV group.[26] However, in 2019, Thille et al found conflicting results.[27] In their RCT, they noted a lower re-intubation rate and incidence of post-extubation failure in the NIV group compared to the HFNC group. The contradictory results probably can be explained by the way NIV was used in both studies. Thille et al used NIV for longer periods of time, and also used HFNC during breaks from NIV.[27]

A 2019 study demonstrated that compared to oxygen therapy, HFNC prior to intubation in adult patients with hypoxemia reduced intubation-related complications.[28] When compared to NIV, however, HFNC resulted in more desaturation events. Whether using HFNC has any advantages over a manual resuscitator (with a positive end-expiratory pressure [PEEP] valve) or a critical care ventilator (with a mask) remains to be seen. It is not yet known if placing a previously unused HFNC for the purposes of preoxygenation prior to intubation is necessary because of cost and resource availability concerns.[2]

There has been considerable interest in the role of HFNC for the treatment of COPD exacerbations because of the effects of dead space washout on CO_2 and overall patient improvement.[29] Lee et al published an RCT in 2018 that found no differences between the NIV group and the HFNC group in terms of intubation rate and 30-day hospital mortality.[30] This study should be interpreted with caution, however, because the study design was a bit vague. That said, the findings were similar to an observational cohort study published in 2019 (evaluating HFNC vs. NIV in hypercapnic respiratory failure), which found that treatment failure was similar between the modalities.[31] Other studies also suggest that HFNC may be useful as an alternative to NIV in mild to moderate COPD patients, but more high-quality studies are needed.[29,32]

As of 2020, it appears that HFNC can reduce the intubation rate in patients with AHRF. This may be particularly true in patients with milder hypoxemia. Regarding post-extubation, HFNC reduces the risk of developing post-extubation failure, but may not reduce re-intubation rates. For pre-intubation use, HFNC appears to be superior to oxygen therapy, but not better than NIV in terms of desaturation events. Finally, HFNC might be useful as a substitute to NIV in mild to moderate COPD.

Regardless of the many published studies to date, a great deal of uncertainty remains. It is difficult to interpret HFNC literature because of the variations in devices (high flow vs. high velocity), disease conditions, settings (flow, FiO_2), duration of treatment, and comparators. HFNC certainly plays an important role in the critical care setting, but the timing, duration, management, and weaning from HFNC needs further study. Additionally, a theoretical advantage of HFNC over NIV is that it allows patients to eat and drink while on the device. This is concerning, as the impact of HFNC oxygen therapy on swallow function has not been investigated thoroughly. This deserves more study so that clinicians can have confidence when deciding to allow patients to eat or drink. Finally, the best way to initiate, manage, and titrate HFNC is not known, so clinical practice varies widely. It is reasonable to apply the highest flow tolerable to the patient in an effort to maximize the physiologic effects of HFNC.

At least in theory, this would allow for the FiO_2 to be titrated to meet oxygenation goals, although this, too, deserves more study.

HFNC AND COVID-19

For patients with COVID-19, HFNC oxygen therapy may be a suitable way to improve oxygenation and reduce the need for endotracheal intubation.[34-40] While the data are relatively limited at this time, available evidence suggests HFNC is used commonly in patients with COVID-19-related respiratory distress.[40] In a retrospective observational study of HFNC use in two hospitals in China, Wang et al noted that HFNC was used more commonly than NIV and invasive mechanical ventilation as a first-line therapy.[40] Not surprisingly, they found a higher HFNC failure rate (7/11, [63%]) in patients with lower PaO_2/FiO_2 ratios (≤ 200 mmHg) compared to the failure rate (0/6, [0%]) in those with a higher PaO_2/FiO_2 ratio (> 200 mmHg).[40]

An interesting use of HFNC is combining it with the effects of prone positioning on oxygenation. Slessarev et al reported in an editorial their experiences with this combination therapy to treat a patient with COVID-19.[35] They found an overall positive result of having their patient self-prone (approximately 16-18 hours/day), which included avoidance of intubation. Elharrar et al found in their prospective, single-center, before-after study of awake, non-intubated patients that 63% of patients were able to tolerate prone positioning for more than three hours.[41] However, it should be noted that oxygenation did not increase in all patients after prone positioning. In fact, only six of 24 patients were considered responders to prone positioning, defined by a partial pressure of arterial oxygen (PaO_2) increase ≥ 20% between before and during prone positioning.

Currently, an RCT is underway comparing HFNC alone to HFNC plus prone positioning for patients with COVID-19-induced moderate to severe acute respiratory distress syndrome (ARDS) (ClinicalTrials.gov Identifier: NCT04325906). It is hoped that this trial and others will provide clarity on whether HFNC alone is sufficient or should be combined with prone positioning as tolerated for patients with COVID-19.

There is reasonable concern about using HFNC during the COVID-19 pandemic because of bio-aerosol dispersion and virus transmission. According to Li et al, studies show that when compared to oxygen therapy delivered via a mask interface, HFNC does not increase environmental microbacterial contamination.[42-44] However, efforts to mitigate risk to healthcare providers should be taken (e.g., wearing adequate personal protective equipment, using negative pressure rooms if available, using portable high-efficiency particulate air filters if negative pressure rooms are unavailable) when HFNC oxygen therapy is used for a patient with COVID-19.[37]

SUMMARY

HFNC is an effective therapeutic modality used to treat acute respiratory failure. It combines comfort and tolerability with multiple physiologic effects, making it a reasonable first-line or alternative modality for a variety of conditions.

Although the evidence to support HFNC oxygen therapy is evolving, many questions remain. Future studies are needed to better understand how to initiate, manage, and titrate HFNC properly for various clinical conditions. ■

REFERENCES

1. Nishimura M. High-flow nasal cannula oxygen therapy in adults: Physiological benefits, indication, clinical benefits, and adverse effects. *Respir Care* 2016;61:529-541.
2. Li J, Jing G, Scott JB. Year in Review 2019: High-flow nasal cannula oxygen therapy for adult subjects. *Respir Care* 2020;65:545-557.
3. Schwabbauer N, Berg B, Blumenstock G, et al. Nasal high-flow oxygen therapy in patients with hypoxic respiratory failure: Effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). *BMC Anesthesiol* 2014;14:66.
4. Peters SG, Holets SR, Gay PC. High-flow nasal cannula therapy in do-not-intubate patients with hypoxemic respiratory distress. *Respir Care* 2013;58:597-600.
5. Calvano TP, Sill JM, Kemp KR, Chung KK. Use of a high-flow oxygen delivery system in a critically ill patient with dementia. *Respir Care* 2008;53:1739-1743.
6. Drake MG. High-flow nasal cannula oxygen in adults: An evidence-based assessment. *Ann Am Thorac Soc* 2018;15:145-155.
7. Corley A, Caruana LR, Barnett AG, et al. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth* 2011;107:998-1004.
8. Riera J, Pérez P, Cortés J, et al. Effect of high-flow nasal cannula and body position on end-expiratory lung volume: A cohort study using electrical impedance tomography. *Respir Care* 2013;58:589-596.
9. Parke RL, Bloch A, McGuinness SP. Effect of very-high-flow nasal therapy on airway pressure and end-expiratory lung impedance in healthy volunteers. *Respir Care* 2015;60:1397-1403.
10. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care* 2013;58:1621-1624.
11. Nishimura M. High-flow nasal cannula oxygen therapy devices. *Respir Care* 2019;64:735-742.
12. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: Mechanisms of action. *Respir Med* 2009;103:1400-1405.
13. Sun Y-H, Dai B, Peng Y, et al. Factors affecting FiO_2 and PEEP

during high-flow nasal cannula oxygen therapy: A bench study. *Clin Respir J* 2019;13:758-764.
14. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults: Mechanisms of action and clinical implications. *Chest* 2015;148:253-261.
15. Delorme M, Bouchard PA, Simon M, et al. Physiologic effects of high-flow nasal cannula in healthy subjects. *Respir Care* 2020; April 14. doi: 10.4187/respcare.07306 [Online ahead of print].
16. Azoulay E, Lemiale V, Mokart D, et al. Effect of high-flow nasal oxygen vs standard oxygen on 28-day mortality in immunocompromised patients with acute respiratory failure: The HIGH randomized clinical trial. *JAMA* 2018;320:2099-2107.
17. Rochwerg B, Granton D, Wang DX, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: A systematic review and meta-analysis. *Intensive Care Med* 2019;45:563-572.
18. Shen Y, Cai G, Yan J. Effect of high flow nasal cannula therapy may be modified by PaO2/FIO2 ratio in acute hypoxemic respiratory failure. *Intensive Care Med* 2019;45:1169-1170.
19. Tinelli V, Cabrini L, Fominskiy E, et al. High flow nasal cannula oxygen vs. conventional oxygen therapy and noninvasive ventilation in emergency department patients: A systematic review and meta-analysis. *J Emerg Med* 2019;57:322-328.
20. Zhu Y, Yin H, Zhang R, et al. High-flow nasal cannula oxygen therapy versus conventional oxygen therapy in patients after planned extubation: A systematic review and meta-analysis. *Crit Care* 2019;23:180.
21. Vourc'h M, Nicolet J, Volteau C, et al. High-flow therapy by nasal cannulae versus high-flow face mask in severe hypoxemia after cardiac surgery: A single-center randomized controlled study — The HEART FLOW study. *J Cardiothorac Vasc Anesth* 2020;34:157-165.
22. Zochios V, Collier T, Blaudszun G, et al. The effect of high-flow nasal oxygen on hospital length of stay in cardiac surgical patients at high risk for respiratory complications: A randomised controlled trial. *Anaesthesia* 2018;73:1478-1488.
23. Ferrando C, Puig J, Serralta F, et al. High-flow nasal cannula oxygenation reduces postoperative hypoxemia in morbidly obese patients: A randomized controlled trial. *Minerva Anestesiol* 2019;85:1062-1070.
24. Futier E, Paugam-Burtz C, Godet T, et al. Effect of early postextubation high-flow nasal cannula vs conventional oxygen therapy on hypoxaemia in patients after major abdominal surgery: A French multicentre randomised controlled trial (OPERA). *Intensive Care Med* 2016;42:1888-1898.
25. Corley A, Bull T, Spooner AJ, et al. Direct extubation onto high-flow nasal cannulae post-cardiac surgery versus standard treatment in patients with a BMI ≥ 30: A randomised controlled trial. *Intensive Care Med* 2015;41:887-894.
26. Hernandez G, Vaquero C, Colinas L, et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: A randomized clinical trial. *JAMA* 2016;316:1565-1574.
27. Thille AW, Muller G, Gacouin A, et al. Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: A randomized clinical trial. *JAMA* 2019;322:1465-1475.
28. Fong KM, Au SY, Ng GWY. Preoxygenation before intubation in adult patients with acute hypoxemic respiratory failure: A network meta-analysis of randomized trials. *Crit Care* 2019;23:319.
29. Pisani L, Astuto M, Prediletto I, Longhini F. High flow through nasal cannula in exacerbated COPD patients: A systematic review. *Pulmonology* 2019;25:348-354.
30. Lee MK, Choi J, Park B, et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. *Clin Respir J* 2018;12:2046-2056.
31. Sun J, Li Y, Ling B, et al. High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: An observational cohort study. *Int J Chron Obstruct Pulmon Dis* 2019;14:1229-1237.
32. Longhini F, Pisani L, Lungu R, et al. High-flow oxygen therapy after noninvasive ventilation interruption in patients recovering from hypercapnic acute respiratory failure: A physiological crossover trial. *Crit Care Med* 2019;47:e506-e511.
33. Boccatonda A, Groff P. High-flow nasal cannula oxygenation utilization in respiratory failure. *Eur J Intern Med* 2019;64:10-14.
34. Rali AS, Nunna KR, Howard C, et al. High-flow nasal cannula oxygenation revisited in COVID-19. *Card Fail Rev* 2020;6:e08.
35. Slessarev M, Cheng J, Ondrejicka M, Arntfield R; Critical Care Western Research Group. Patient self-proning with high-flow nasal cannula improves oxygenation in COVID-19 pneumonia. *Can J Anaesth* 2020 Apr 21;1-3.
36. Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress syndrome from COVID-19. *Lancet Respir Med* 2020;8:433-434.
37. Lyons C, Callaghan M. The use of high-flow nasal oxygen in COVID-19. *Anaesthesia* 2020;75:843-847.
38. Geng S, Mei Q, Zhu C, et al. High flow nasal cannula is a good treatment option for COVID-19. *Heart Lung* 2020;S0147-9563(20)30113-8.
39. Li L, Li R, Wu Z, et al. Therapeutic strategies for critically ill patients with COVID-19. *Ann Intensive Care* 2020;10:45.
40. Wang K, Zhao W, Li J, et al. The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China. *Ann Intensive Care* 2020;10:37.
41. Elharrar X, Trigui Y, Dols AM, et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA* 2020;e208255.
42. Li J, Fink JB, Ehrmann S. High-flow nasal cannula for COVID-19 patients: Low risk of bio-aerosol dispersion. *Eur Respir J* 2020;55:2000892.
43. Leung CCH, Joynt GM, Gomersall CD, et al. Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: A randomized controlled crossover trial. *J Hosp Infect* 2019;101:84-87.
44. Ip M, Tang JW, Hui DS, et al. Airflow and droplet spreading around oxygen masks: A simulation model for infection control research. *Am J Infect Control* 2007;35:684-689.

ABSTRACT & COMMENTARY

Preventing Post-Extubation Respiratory Failure: Can We Decrease Risk in our High-Risk Populations?

By Kathryn Radigan, MD, MSc

Attending Physician, Division of Pulmonary and Critical Care, Stroger Hospital of Cook County, Chicago

Dr. Radigan reports no financial relationships relevant to this field of study.

SYNOPSIS: A multicenter, randomized clinical trial of 641 adults deemed ready for weaning after at least 24 hours of mechanical ventilation revealed that the use of high-flow nasal oxygen (HFNO) with noninvasive ventilation immediately after extubation significantly decreased the risk of reintubation compared to HFNO alone in mechanically ventilated patients who were at high risk of extubation failure.

SOURCE: Thille AW, Muller G, Gacouin A, et al. Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: A randomized clinical trial. *JAMA* 2019;322:1465-1475.

Thille and colleagues conducted a multicenter, randomized clinical trial in 30 intensive care units (ICUs) in France between April 2017 and January 2018. The study involved 641 patients who were intubated more than 24 hours in the ICU, were ready for extubation after a successful spontaneous breathing trial, and were deemed high risk for extubation failure (i.e., > 65 years of age or with underlying cardiac or respiratory disease). Participants were randomly assigned to high-flow nasal oxygen (HFNO) alone (n = 306) or HFNO with noninvasive ventilation (NIV) (n = 342) immediately after extubation. Underlying chronic cardiac diseases included left ventricular dysfunction (left ventricular ejection fraction < 45%), history of cardiogenic pulmonary edema, ischemic heart disease, or permanent atrial fibrillation. Underlying chronic lung diseases included chronic obstructive pulmonary disease, obesity-hypoventilation syndrome, or restrictive pulmonary disease. Exclusion criteria included long-term treatment with NIV at home, contraindication to NIV, underlying neuromuscular disease, traumatic brain injury leading to intubation, patients with unplanned extubation (accidental or self-extubation), or patients with a do-not-reintubate order at the time of extubation.

Patients in the control group were treated continuously with HFNO for at least 48 hours with a flow of 50 L/min and fraction of inspired oxygen (FiO_2) adjusted to maintain an oxygen saturation (SpO_2) of at least 92%. Patients in the NIV intervention group were treated with NIV immediately after extubation, with a minimal duration of at least 12 hours per day during the 48 hours after extubation and specific attention to adherence at night. When the patient was not on NIV, HFNO was delivered. Both groups were treated for a minimum of 48 hours.

In terms of the primary outcome, on day 7, the reintubation rate was 11.8% (95% confidence interval [CI], 8.4% to 15.2%) in the NIV/HFNO group vs. 18.2% (95% CI, 13.9% to 22.6%) in the HFNO-only group (difference, –6.4%; 95% CI, –12.0% to –0.9%; $P = 0.02$). As for secondary outcomes, the proportion of patients with post-extubation respiratory failure at day 7 was significantly lower in the NIV/HFNO group (21% vs. 29%; $P = 0.01$), and reintubation rates up until ICU discharge also were lower in this group (12% vs. 20%; $P = 0.009$) compared to the HFNO-only group. However, ICU mortality rates were not significantly different: 6% in the NIV/HFNO group vs. 9% in the HFNO group ($P = 0.25$).

■ COMMENTARY

Successful liberation from mechanical ventilation on the first attempt without the need for reintubation is important. Approximately 10% to 15% of all patients extubated will fail, with higher numbers for those at particularly increased risk.[1] In these patients at particularly increased risk, the mortality is 25% to 50%.[2] To reduce risk, the most recent international practice guidelines published in 2017 made a conditional recommendation (low certainty of evidence) to use NIV to prevent post-extubation respiratory failure for high-risk patients, but recommended against NIV in low-risk patients and in those who develop post-extubation respiratory failure.[3] Shortly before this recommendation, Hernández and colleagues revealed that HFNO prevents post-extubation respiratory failure and reintubation in the critically ill, specifically those

patients at low risk of reintubation.[4] Six months later, the same group showed that HFNO therapy was not inferior to NIV for preventing reintubation and post-extubation respiratory failure in high-risk patients.[5] Of course, the question of whether NIV plus HFNO was better than HFNO alone sparks an interesting clinical question, especially since the clinical evidence supporting NIV was not profound. In this study, Thille and colleagues found that NIV with HFNO reduced the risk of reintubation at seven days post-extubation, but also up until ICU discharge.

The study's protocol for administering NIV and HFNO was significant in the amount of time patients spent on NIV. Patients assigned to the NIV intervention group were started on NIV immediately after extubation. The first session lasted at least four hours, with a minimal duration of at least 12 hours per day during the 48 hours following extubation, with continuous application of NIV throughout the entire night period. The NIV/HFNO group was successful in maintaining a mean of 13 hours of NIV time within the first 24 hours. NIV was delivered with an ICU ventilator with NIV mode or a dedicated bilevel ventilator in pressure support (PS) mode with a minimal PS of 5 cm H_2O targeting a tidal volume of 6-8 mL/kg of predicted body weight, a positive end-expiratory pressure (PEEP) level of 5-10 cm H_2O, and an FiO_2 targeted to $SpO_2 \geq 92\%$. When NIV was not in use, HFNO was delivered as within the control group. Both groups continued for at least 48 hours, but the treatment was continued until there were no signs of respiratory failure. Although the control group was only supposed to receive HFNO, it is important to note that 20 out of 70 patients who experienced post-extubation respiratory failure also received NIV as a rescue therapy for a mean of seven hours. Ten of these patients needed reintubation.

The real secret to this study was how the investigators achieved high adherence to the protocol, with only 6% of patients not tolerating NIV. One may question whether the high adherence was the result of the use of HFNO during the off time. The NIV/HFNO group benefits from both delivery systems. NIV assists ventilation by providing pressurized oxygenated gas to the airways through a tight-fitting facial mask. Although NIV is effective in offsetting the load of acute illness, it also may be poorly tolerated because of discomfort or claustrophobia, inadequate secretion clearance, and poor synchrony as a result of high respiratory rate and minute ventilation in patients with acute respiratory failure. This often leads to high inspiratory and expiratory pressures and predisposes the patient to increased air leaks and the need for a tighter fit, leading to more discomfort. The ability to offset this with HFNO, which is more comfortable because the high flow rates are closer to the patient's flow rate, is a great alternative.[6] The HFNO system also can flush out anatomical dead space in the nasopharynx and upper airway and keep secretions moist, promoting mobilization. Even patients with hypercapnia in addition to hypoxemia may benefit from the combination of upper airway CO_2 clearance and decreased CO_2 production from reduced metabolic demand. The balance between NIV's ability to offset the load of acute illness with the comforts and benefits of HFNO likely led to the successful outcomes and optimal NIV adherence.

Interestingly, there was no significant interaction between partial pressure of carbon dioxide ($PaCO_2$) at enrollment and treatment group with respect to reintubation ($P = 0.25$). The number of patients with elevated $PaCO_2$ was evenly distributed between the NIV/HFNO and HFNO groups. Patients with $PaCO_2$ > 45 mmHg before extubation had a significantly lower reintubation rate at day 7 with NIV/HFNO than with HFNO alone (8% vs. 21%; $P = 0.049$). The findings at seven days are not surprising, especially since there are data showing that prophylactic NIV in hypercapnic patients resulted in lower rates of respiratory failure and mortality after extubation.[7]

This study supports the use of NIV with HFNO immediately after extubation because it significantly decreased the risk of reintubation compared HFNO alone in patients who were mechanically ventilated and at high risk of extubation failure. This finding was most profound for hypercapnic patients, and appropriate clinical judgment should be used decide which patients within the high-risk, non-hypercapnic group will benefit the most. In the future, it would be interesting to explore the differences in outcomes between patients with chronic cardiac vs. pulmonary disease and aim for larger randomized controlled trials that could evaluate mortality as a primary outcome. ■

REFERENCES

1. Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 2013;187:1294-1302.
2. Thille AW, Boissier F, Ben Ghezala H, et al. Risk factors for and prediction by caregivers of extubation failure in ICU patients: A prospective study. *Crit Care Med* 2015;43:613-620.
3. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: Noninvasive ventilation for acute respiratory failure. *Eur Respir J* 2017;50:1602426.
4. Hernàndez G, Vaquero C, Gonzalez P, et al. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: A randomized clinical trial. *JAMA* 2016;315:1354-1361.
5. Hernàndez G, Vaquero C, Colinas L, et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: A randomized clinical trial. *JAMA* 2016;316:1565-1574.

6. Drake MG. High-flow nasal cannula oxygen in adults: An evidence-based assessment. *Ann Am Thorac Soc* 2018;15:145-155.

7. Ferrer M, Sellares J, Valencia M, et al. Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: Randomised controlled trial. *Lancet* 2009;374:1082-1088.

CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the provided references for further research.

2. Log on to **ReliasMedia.com** and click on My Account. First-time users must register on the site. Tests are taken after each issue.

3. Pass the online test with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.

4. After successfully completing the test, your browser will be automatically directed to the activity evaluation form, which you will submit online.

5. Once the completed evaluation is received, a credit letter will be emailed to you.

CME/CE QUESTIONS

1. **Regarding the physiologic effects of high-flow nasal cannula (HFNC), which of the following statements is true?**
   a. The positive pressure generated by HFNC is unaffected by mouth opening/closure.
   b. HFNC can deliver well-conditioned (heated and humidified) gases as long as device flow is higher than patient inspiratory flow.
   c. The actual FiO_2 delivered to a patient is always what is set on the device.
   d. The washout of anatomic dead space by HFNC generally increases patient breathing effort and worsens patient comfort.

2. **HFNC prior to intubation may be more effective at reducing intubation-related complications in adult patients with hypoxemia when compared to which of the following?**
   a. Noninvasive ventilation
   b. Standard oxygen therapy
   c. Manual resuscitator with positive end-expiratory pressure (PEEP) valve
   d. Critical care ventilator with a mask

3. **In the trial by Thille et al, which modality significantly decreased the risk of reintubation when used immediately after extubation in patients at high risk of extubation failure?**
   a. Noninvasive ventilation
   b. Low-flow nasal cannula
   c. High-flow nasal with noninvasive ventilation
   d. Low-flow nasal cannula with noninvasive ventilation

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.