KEY ADVANCES
PRACTICE ADVANCE

Noninvasive Respiratory Support for Acute Hypoxemic Respiratory Failure

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Why is this topic important? Acute respiratory failure is common in adults presenting to the emergency department (ED). An ideal means of respiratory support is noninvasive, reduces the rate of intubation, and improves mortality.

How will this change my clinical practice? Studies comparing nasal high-flow (NHF) systems with noninvasive positive pressure ventilation (NIPPV) have not proven a consistent difference in mortality or need for intubation among patients with acute hypoxemic or hypercapnic respiratory failure. Based on available literature, NHF systems have a role in appropriately selected patients.

Synopsis Focus Points:

- **NHF provides heated, humidified gas and a set fraction of inspired oxygen and flow and can reduce dead space and potentially work of breathing.**
- **NHF or NIPPV is a reasonable option for first-line noninvasive respiratory support in patients with acute hypoxemic respiratory failure. NHF is also an option in those with acute chronic obstructive pulmonary exacerbation or acute decompensated heart failure.**
- **NHF should be started at higher flow rates to reduce lung strain and work of breathing. Weaning the patient once improved is recommended, rather than titrating from low to high, if the patient worsens.**
- **Close monitoring of any patient on noninvasive respiratory support is necessary. Unsuccessful noninvasive respiratory support is associated with increased mortality. Patients who fail to improve likely require endotracheal intubation.**

Background:

Acute respiratory failure has a variety of etiologies and requires emergent management. Several modalities may assist with airway and respiratory support, known as noninvasive respiratory support (NRS). NRS can be divided into NIPPV, which is based on pressure, and NHF systems, which are based on flow. NIPPV has been shown to be effective at preventing intubation and improving outcomes in patients with acute hypercapnic or hypercapnic and hypoxemic respiratory failure, specifically exacerbations of chronic obstructive pulmonary disease (COPD), asthma, and acute decompensated heart failure (ADHF), but its use is controversial when respiratory failure is secondary to other etiologies, including acute lung injury or infection.

NHF systems provide humidified and heated gas at a set fraction of inspired oxygen (FiO_2) and a set flow of air (often at 30-70 L/min). This can improve mucociliary clearance, gas exchange, and oxygenation while reducing work of breathing.(1-4) Due to these effects, there are several potential uses for NHF, particularly those with acute hypoxemic respiratory failure (AHRF).

Indications:

Acute hypoxemic respiratory failure

AHRF is associated with parenchymal airspace disease from inflammation or infection. NHF has several advantages in AHRF, as it can support oxygenation and ventilation with flow-dependent effects while avoiding excess pressure.(3,4) A seminal randomized controlled trial (RCT) published in 2015 that compared NHF, NIPPV, and standard oxygen in AHRF found greater risk of death at 90 days in those receiving standard oxygen (hazard ratio HR = 2.01; 95% CI 1.01 to 3.99) or NIPPV (HR = 2.50; 95% CI 1.31 to 4.78) versus NHF systems, although there was no difference in rates of intubation.(5) While subsequent studies conducted in patients with COVID-19 have demonstrated conflicting results,(6,7) a meta-analysis comparing face mask NIPPV and NHF found no difference in mortality or intubation.(8) Although it is currently unclear whether a certain subset of patients with AHRF would benefit more from either NHF or NIPPV, the 2021 Surviving Sepsis Campaign guidelines recommended use of NHF over other NIPPV modalities.(9) NHF may also assist in those with pneumonia or hemoptysis who demonstrate hypoxemia or increased work of breathing, as NHF allows for clearance of any secretions.

COPD, Asthma, and Hypercapnic Respiratory Failure

In patients with COPD or asthma exacerbation, airway collapse may result in air trapping, hyperinflation, and increased work of breathing.(4) NIPPV can reduce inspiratory and expiratory effort and work of breathing in these patients and is currently considered the standard of care for those with COPD exacerbation.(10) However, NHF may also assist, as it may flush the airway dead space and increase end-expiratory lung volumes, ultimately reducing inspiratory effort and the work of breathing.(11,12) A meta-analysis comparing NIPPV and NHF in those with acute COPD exacerbation found no difference in mortality or rates of treatment failure,(11) and a multicenter trial found NHF was noninferior to NIPPV in reducing partial pressure of carbon dioxide ($PaCO_2$) at 2 hours.(12) A subgroup analysis found $PaCO_2$, pH, intubation rates, and treatment failure rates were similar between NHF and NIPPV in patients with hypercapnia,(13) and another study found NHF reduced $PaCO_2$ in hypercapnic patients with pneumonia and COPD.(14)

While it has been hypothesized that NHF does not provide enough ventilatory support to be as useful as NIPPV in hypercapnic respiratory failure, a meta-analysis of 8 RCTs (N = 528) found no difference between NHF and NIPPV, with NHF demonstrating a relative risk of 0.86 (95% CI 0.48 to 1.56) for mortality and 0.80 (95% CI 0.46 to 1.39) for intubation compared to NIPPV.(11)

Importantly, guidelines recommend NIPPV for patients with COPD exacerbation, hypercapnia, and respiratory acidosis.(15) If the undifferentiated patient in the ED has increased work of breathing but does not have severe respiratory acidosis, NHF may be considered. While NHF can be considered in patients with significant work of breathing and respiratory acidemia, NIPPV may be necessary, targeting a higher inspiratory positive airway pressure and lower expiratory positive airway pressure.

Decompensated heart failure
ADHF is associated with elevated pulmonary venous pressures resulting in pulmonary edema, hypoxemia, and increased work of breathing. NIPPV has traditionally been used in this setting and is associated with reduced need for intubation, work of breathing, and mortality.(4) NHF has also been used to treat ADHF, and recent studies suggest NHF is a viable option for managing ADHF.(16,17) NHF can increase end-expiratory lung volumes, which may improve lung mechanics and gas exchange in those with ADHF.

Using NHF:

When using NHF, it is recommended to start with higher flows to assist with oxygenation and work of breathing and wean as the patient improves. This contrasts with titrating up the flow as the patient worsens. NRS success reduces work of breathing and mortality, but NRS failure is associated with increased mortality.(18-20) Therefore, frequent patient reassessment is necessary, no matter which NRS modality is used. Studies have sought to predict NRS failure. The ROX index ([SpO2/FiO2] / respiratory rate) has demonstrated promise, with values > 4.88 predictive of not requiring intubation, and values < 2.85 at 2 hours, < 3.47 at 6 hours, and < 3.85 at 12 hours predict NHF failure.(21) Patients with multiorgan failure are also more likely to fail NRS. If the patient's respiratory status fails to improve with NRS, endotracheal intubation is recommended.

This is level 1a evidence.(22)

References:

1. Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. *Br J Anaesth.* 2009;103(6):886-890. doi:10.1093/BJA/AEP280. https://www.bjanaesthesia.org/article/S0007-0912(17)33885-0/fulltext
2. Möller W, Feng S, Domanski U, et al. Nasal high flow reduces dead space. *J Appl Physiol (1985).* 2017;122(1):191-197. doi:10.1152/JAPPLPHYSIOL.00584.2016. https://journals.physiology.org/doi/full/10.1152/japplphysiol.00584.2016
3. Mauri T, Turrini C, Eronia N, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med.* 2017;195(9):1207-1215. doi:10.1164/RCCM.201605-0916OC. https://www.atsjournals.org/doi/pdf/10.1164/rccm.201605-0916OC
4. Mosier JM, Tidswell M, Wang HE. Noninvasive respiratory support in the emergency department: Controversies and state-of-the-art recommendations. *J Am Coll Emerg Physicians Open.* 2024 Mar 7;5(2):e13118. doi: 10.1002/emp2.13118.
5. Frat J-P, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med.* 2015;372(23):2185-2196. doi:10.1056/NEJMOA150332. https://www.nejm.org/doi/full/10.1056/NEJMoa1503326

6. Perkins GD, Ji C, Connolly BA, et al. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. *JAMA*. 2022;327(6):546-558. doi:10.1001/jama.2022.0028
7. Nagata K, Yokoyama T, Tsugitomi R, et al. Continuous positive airway pressure versus high-flow nasal cannula oxygen therapy for acute hypoxemic respiratory failure: a randomized controlled trial. *Respirology*. 2024;29(1):36-45. doi:10.1111/resp.14588
8. Chaudhuri D, Trivedi V, Lewis K, Rochwerg B. High-flow nasal cannula compared with noninvasive positive pressure ventilation in acute hypoxic respiratory failure: a systematic review and meta-analysis. *Crit Care Explor.* 2023;5(4):e0892.
9. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med.* 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y.
10. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med.* 1995;333(13):817-822.
11. Ovtcharenko N, Ho E, Alhazzani W, et al. High-flow nasal cannula versus non-invasive ventilation for acute hypercapnic respiratory failure in adults: a systematic review and meta-analysis of randomized trials. *Crit Care*. 2022;26(1):348. doi:10.1186/s13054-022-04218-3.
12. Cortegiani A, Longhini F, Madotto F, et al. High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial. *Crit Care.* 2020;24(1):692.
13. Doshi PB, Whittle JS, Dungan G, et al. The ventilatory effect of high velocity nasal insufflation compared to non-invasive positive pressure ventilation in the treatment of hypercapneic respiratory failure: a subgroup analysis. *Heart Lung.* 2020;49(5):610-615.
14. Kim ES, Lee H, Kim SJ, et al. Effectiveness of high-flow nasal cannula oxygen therapy for acute respiratory failure with hypercapnia. *J Thoracic Dis.* 2018;10(2):882-888.
15. 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(2):1602426.
16. Ko DR, Beom J, Lee HS, et al. Benefits of high-flow nasal cannula therapy for acute pulmonary edema in patients with heart failure in the emergency department: a prospective multi-center randomized controlled trial. *J Clin Med.* 2020;9(6):1937.
17. Makdee O, Monsomboon A, Surabenjawong U, et al. High-flow nasal cannula versus conventional oxygen therapy in emergency department patients with cardiogenic pulmonary edema: a randomized controlled trial. *Ann Emerg Med.* 2017;70(4):465-472.e2.
18. Bellani G, Laffey JG, Pham T, et al. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE Study. *Am J Respir Crit Care Med.* 2017;195(1):67-77.
19. Carteaux G, Millan-Guilarte T, De Prost N, et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. *Crit Care Med.* 2016;44(2):282-290.
20. Grieco DL, Menga LS, Raggi V, et al. Physiological comparison of high-flow nasal cannula and helmet noninvasive ventilation in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med.* 2020;201(3):303-312.
21. Roca O, Caralt B, Messika J, et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. *Am J Respir Crit Care Med.* 2019;199(11):1368-1376.
22. Oxford Centre for Evidence-Based Medicine: levels of evidence (March 2009). Centre for Evidence-Based Medicine. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

Resources for additional learning:

https://emcrit.org/pulmcrit/pulmcrit-does-the-high-trial-debunk-high-flow-nasal-cannula/

https://emcrit.org/ibcc/support/

https://emcrit.org/pulmcrit/bipap-hfnc/

https://www.thesgem.com/2015/11/sgem135-the-answer-my-friend-is-blowin-in-your-nose-high-flow-nasal-oxygen/

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