

## Evidence-based practice for noninvasive ventilation and high flow nasal cannula: a summary of the literature

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### Topics included

- COPD exacerbation
- Community-acquired pneumonia
- Immunocompromised patients
- Hypoxemic respiratory failure
- Cardiogenic pulmonary edema
- Post-extubation (immediate)
- Postoperative patients

### Topics excluded

- Extubation failure
- Do not intubate/resuscitate
- Acute asthma
- Pre-intubation oxygenation

### Executive summary of the current landscape

Noninvasive clinical scenario	NIV	HFNC	
COPD exacerbation (pH 7.25–7.35)	Highly recommended	No data	Highly recommended
Community-acquired pneumonia	Mixed evidence *	Recommended	Recommended
Immunocompromised patients	Recommended	Recommended	Recommended
<b>Hypoxemic respiratory failure</b>			
PaO <sub>2</sub> /FiO <sub>2</sub> 200–300	Recommended	Recommended	Recommended
PaO <sub>2</sub> /FiO <sub>2</sub> < 200	High risk	Recommended	Recommended
Cardiogenic pulmonary edema	Highly recommended	No data	No data
Post-extubation for high-risk patients (immediately post)	Recommended	Recommended	Recommended
Post-extubation with COPD (early liberation)	Recommended	No data	No data
Postoperative patients	Recommended	Inferior	Inferior

\* Mixed evidence exists in this category, without a clear consensus in the literature. Monitor patients closely and consider the presence of other risk factors.

Recommendations based on the author's review of the currently available literature, including existing guidelines.

## Key risk factors of treatment failure<sup>32-35</sup>

- High severity of illness score
  - SOFA, SAPS II, APACHE
- Use of vasopressors (shock)
- Low PaO<sub>2</sub>/FiO<sub>2</sub> ratio (< 150)
- ARDS severity on initial assessment
- SpO<sub>2</sub> < 90% for > 5 min
- pH < 7.25 (COPD) pH < 7.35 (hypoxemic RF)
- Older age
- Tidal volume > 9.5 ml/kg of PBW
- HACOR score > 5 (needs further validation)
- Level of consciousness
- Failure to improve within 1-2 hour

**Early intervention and close monitoring of risk factors before and after NIV are extremely important. Delaying intubation in ANY patient is strongly discouraged and leads to poor outcomes.**<sup>7,14-16,36</sup>

## Evidence summary

### COPD exacerbation

#### NIV

The current evidence continues to strongly support the use of NIV for the treatment of COPD exacerbation. There is an early Cochrane Review from 2004 that analyzed 14 studies,<sup>1</sup> and clinical practice guidelines that reviewed 16 randomized controlled trials.<sup>2</sup> The use of NIV to treat COPD exacerbation results in less intubation (treatment failure) and lower mortality compared to standard treatment (traditional oxygen therapy, and pharmacological agents).

Benefits are mostly related to the severity of COPD, particularly in patients with a pH < 7.35 with relative hypercarbia. Patients with a pH > 7.35 are less likely to show a significant difference in clinical outcomes when treated with NIV.<sup>2</sup>

#### HFNC

Currently there is minimal data regarding HFNC use in COPD patients (without exacerbation), with mixed response. Lower respiratory rates, and lower PaCO<sub>2</sub> levels have been reported in studies.<sup>3,4</sup> However, these patients were not in an acute exacerbation, and patients with pH < 7.35 were excluded.<sup>5</sup> A case study demonstrated successful management of a patient with a pH of 7.31 who refused NIV. However, case studies are the lowest form of evidence and should not be generalized to clinical practice.<sup>4</sup>

### Community-acquired pneumonia

#### NIV

Early studies assessing the effect of NIV to treat community-acquired pneumonia (CAP) are conflicting and of low quality.<sup>2</sup> More recent studies have demonstrated high failure rates of NIV, and NIV failure was associated with higher mortality.<sup>6,7</sup> Another study found in an adjusted analysis that NIV failure patients had worse outcomes than patients invasively ventilated as first-line therapy.<sup>8</sup> The close monitoring of these patients is key to successful treatment. Delaying intubation was also associated with higher mortality.<sup>7</sup>

#### HFNC

There appears to be no studies assessing the use of HFNC in CAP specifically. The FLORALI study had a significant number of CAP patients enrolled in the study, but there is currently no subgroup analysis of the CAP patients. However, the HFNC patients had lower 90-day mortality.<sup>6</sup>

### Immunocompromised patients

#### NIV

Early data with a moderate quality of evidence suggested benefits using NIV over standard oxygen therapy for treating immunocompromised patients presenting with hypoxemic respiratory failure (preventing invasive ventilation is preferred when mortality risk is high).<sup>2</sup> However, a recent study showed no difference in outcomes comparing NIV with standard oxygen therapy.<sup>9</sup>

#### HFNC

A recent study looked at NIV versus HFNC in the management of immunocompromised patients with hypoxic respiratory failure, with results favoring HFNC.<sup>10</sup> In a recent post-hoc analysis of immunocompromised patients in the FLORALI trial, age and the use of NIV as first-line therapy was associated with needing intubation and higher mortality, therefore HFNC would be the preferred option.<sup>11</sup>

### Hypoxemic respiratory failure

#### NIV

Early meta-analyses on the role of NIV in treating hypoxemic respiratory failure demonstrated a risk reduction for endotracheal intubation and mortality.<sup>12,13</sup> However, due to the heterogeneity of the studies, a recommendation for the routine use of NIV with hypoxemic respiratory failure was not recommended. The effectiveness of NIV in patients with hypoxemic respiratory failure is likely related to the specific population of patients, and many studies looked at general acute respiratory failure (including many patients with different etiologies).

Severity of illness, comorbidities, and severity of hypoxemia play a major role in determining the appropriateness of using NIV to prevent intubation.<sup>14</sup> NIV failure has been associated with higher mortality in these patients. Delaying intubation is a key contributor to worse outcomes.<sup>14-16</sup>

## **ARDS patients**

Treating patients with acute respiratory distress syndrome (ARDS) using NIV has long been controversial. The current Berlin Definition of ARDS refers to patients with  $\text{PaO}_2/\text{FiO}_2$  200 – 300 as “mild ARDS”, but in previous literature it was referred to as “acute lung injury”.<sup>7,18</sup> The current literature supports the idea that caution needs to be taken with patients with lower  $\text{PaO}_2/\text{FiO}_2$ , particularly in patients with moderate and severe ARDS ( $\text{PaO}_2/\text{FiO}_2 < 200$  and  $< 100$  respectively) as it is associated with a high failure rate, and failure is associated with increased risk of mortality.<sup>17-19</sup> However, patients with mild ARDS can be safely managed with NIV, but HFNC may be preferred.<sup>6,18</sup>

## **ARDS patients – helmet interface**

A randomized controlled trial comparing a helmet interface to the standard full-face mask to deliver NIV in ARDS patients was published in 2016.<sup>20</sup> The control group (standard full-face mask) had a NIV failure rate (intubation rate) of 61.5%, which is comparable to previous studies considering the median  $\text{PaO}_2/\text{FiO}_2$  was quite low at 144.<sup>14</sup> The helmet group had a failure rate of only 18%. The authors suggest this benefit may be related to the ability to apply higher levels of PEEP to the patients using the helmet interface. This was a single center study, the helmet interface is a relatively novel approach, and there is a risk of bias since the groups could not be blinded. However, there was strict criteria for meeting failure/intubation to minimize bias. Further randomized trials with the helmet interface are needed to confirm these results, especially considering the high failure associated with NIV in this population.

## **HFNC**

The previously mentioned FLORALI trial saw a lower, yet insignificant, difference in endotracheal intubation in the overall population of patients with hypoxemic respiratory failure (35% HFNC vs 50% NIV). However, there was a significant difference in intubation rates for patients with a  $\text{PaO}_2/\text{FiO}_2 < 200$  (38% HFNC vs. 58% NIV). The overall 90-day mortality rate was also lower in patients treated with HFNC compared to NIV (hazard ratio for death at 90 days 2.50 [95% CI, to 4.78]). Although ARDS patients were not clearly identified through strict definition, the  $\text{PaO}_2/\text{FiO}_2$  ranges were consistent with the Berlin definition, and they did report that a high percentage of patients enrolled had bilateral infiltrates (75% HFNC, 77% NIV).<sup>6</sup>

## **Cardiogenic pulmonary edema**

### **NIV**

The management of cardiogenic pulmonary edema is well established in the literature. There is a significant reduction in intubation rates and mortality using NIV compared to standard oxygen therapy. Although data suggests there is no difference in outcomes between using CPAP or BiPAP, BiPAP should be used to address any work of breathing, or underlying comorbidities such as COPD.

## **HFNC**

There is currently no evidence to suggest a benefit in managing acute cardiogenic pulmonary edema with HFNC, and therefore should not be used until there is supportive evidence.

## **Post-extubation**

### **NIV – early liberation**

The use of NIV is recommended for centers with NIV expertise to allow for early ventilator liberation in patients with COPD after a failed spontaneous breathing trial, provided there is resolution of underlying cause of respiratory failure (example, infection).<sup>2</sup>

### **NIV – prevent post-extubation failure**

The use of NIV post-extubation is recommended in patients with high risk of extubation failure, but not for patients with low risk of extubation failure.<sup>2</sup>

### **HFNC – prevent post-extubation failure**

There are two randomized trials looking at post-extubation use of HFNC. One study compared HFNC to standard oxygen therapy post-extubation in low risk patients and found a significant reduction in post-extubation failure.<sup>21</sup> The same author compared HFNC to NIV in patients at high risk of post-extubation failure in a non-inferiority randomized trial and found HFNC was not inferior to NIV in patients at high risk of post-extubation failure. The presence of COPD as a risk factor was low and reasonably balanced in both groups. One limitation is that the risk factors for post-extubation failure were quite broad as there is no currently accepted standard in the literature.

## **Postoperative patients**

### **NIV**

The use of NIV has good supportive evidence in post-operative abdominal surgery patients,<sup>23-25</sup> lung resection patients,<sup>25,26</sup> and cardiac surgery patients.<sup>27</sup> The use of NIV resulted in improvements in patient outcomes such as lower reintubation rates and improved oxygenation,<sup>23,24-27</sup> and lower mortality.<sup>26</sup>

### **HFNC**

The use of HFNC has been compared to standard oxygen therapy in cardiac surgery patients with positive effects such as reduced escalation of respiratory support, increased end-expiratory lung impedance, better oxygenation, and lower respiratory rates.<sup>28,29</sup> However, no trials have shown a reduction in intubation rates or other important clinical outcomes in postoperative patients being treated with HFNC.<sup>28-31</sup>

## References

1. Ram F, et al. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *The Cochrane Library*. 2004;3:CD004104.
2. Keenan SP, et al. Clinical practice guidelines for the use of noninvasive positive-pressure ventilation and noninvasive continuous positive airway pressure in the acute care setting. *CMAJ: Canadian Medical Association Journal*. 2011;183.3:E195–214.
3. Pisani I, Comellini V, Nava S. Noninvasive ventilation versus oxygen therapy for the treatment of acute respiratory failure. *Expert review of respiratory medicine*. 2016;10.7:813–21.
4. Millar J, Lutton S, O'Connor P. The use of high-flow nasal oxygen therapy in the management of hypercarbic respiratory failure. *Therapeutic advances in respiratory disease*. 2014;8.2:63–4.
5. Nilius G, et al. Effects of nasal insufflation on arterial gas exchange and breathing pattern in patients with chronic obstructive pulmonary disease and hypercapnic respiratory failure. *Advances in experimental medicine and biology*. 2013;755:26–34.
6. Frat JP, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *The New England Journal of Medicine*. 2015;372.23:2185–2196.
7. Carrillo A, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Medicine*. 2012;38.3:458–466.
8. Murad A, et al. The role of noninvasive positive pressure ventilation in community-acquired pneumonia. *Journal of Critical Care*. 2015;30.1:49–54.
9. Lemiale V, et al. Effect of noninvasive ventilation vs oxygen therapy on mortality among immunocompromised patients with acute respiratory failure: a randomized clinical trial. *JAMA*. 2015;314.16:1711–9.
10. Coudroy R, et al. High-flow nasal cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients with acute respiratory failure: an observational cohort study. *Annals of Intensive Care*. 2016;6.1:45.
11. Frat JP, et al. Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial. *The Lancet. Respiratory Medicine*. 2016;4.8:646–52.
12. Wysocki M, Antonelli M. Noninvasive mechanical ventilation in acute hypoxaemic respiratory failure. *The European Respiratory Journal*. 2001;18.1:209–20.
13. Keenan SP, et al. Does noninvasive positive pressure ventilation improve outcome in acute hypoxemic respiratory failure? A systematic review. *Critical Care Medicine*. 2004;32.12:2516–23.
14. Nava S, Schreiber A, Domenighetti G. Noninvasive ventilation for patients with acute lung injury or acute respiratory distress syndrome. *Respiratory Care*. 2011;56.10:1583–8.
15. Demoule A, et al. Benefits and risks of success or failure of noninvasive ventilation. *Intensive Care Medicine*. 2006;32.11:1756–65.
16. Hraiech S, et al. Time to intubation is associated with outcome in patients with community-acquired pneumonia. *PLoS One*. 2013;8.9:e74937.
17. Force ARDS, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307.23:2526–2533.
18. Xu X, et al. Noninvasive ventilation for acute lung injury a meta-analysis of randomized controlled trials. *Heart & Lung: The Journal of Critical Care*. 2016;45.3:249–57.
19. Chawla R, et al. Acute respiratory distress syndrome: predictors of noninvasive ventilation failure and intensive care unit mortality in clinical practice. *Journal of Critical Care*. 2016;31.1:26–30.
20. Patel B, et al. Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial. *JAMA*. 2016;315.22:2435.
21. Hernández G, 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;315.13:1354.
22. Hernández G, 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;316.15:1565–1574.
23. Squadrone V, et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. *JAMA*. 2005;293.5:589–95.
24. Jaber S, et al. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. *JAMA*. 2016;315.13:1345–53.
25. Chiumello D, Chevillard G, Gregoretti C. Non-invasive ventilation in postoperative patients: a systematic review. *Intensive Care Medicine*. 2011;37.6:918–29.
26. Auriant I, et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. *American Journal Of Respiratory and Critical Care Medicine*. 2001;164.7:1231–5.
27. Zarbock A, et al. Prophylactic nasal continuous positive airway pressure following cardiac surgery protects from postoperative pulmonary complications: a prospective, randomized, controlled trial in 500 patients. *Chest*. 2009;135.5:1252–9.
28. Zhu Y, et al. High-flow nasal cannula oxygen therapy vs conventional oxygen therapy in cardiac surgical patients: a meta-analysis. *Journal of Critical Care*. 2017;38:123–128.
29. Corley A, et al. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *British Journal of Anaesthesia*. 2011;107.6:998–1004.
30. Corley A, et al. Direct extubation onto high-flow nasal cannulae post-cardiac surgery versus standard treatment in patients with a BMI  $\geq$ 30: a randomised controlled trial. *Intensive Care Medicine*. 2015;41.5:887–894.
31. Futier E, 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 Medicine*. 2016;42.12:1888–1898.
32. Duan J, et al. Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict noninvasive ventilation failure in hypoxemic patients. *Intensive Care Medicine*. 2016:1–8.
33. Carreaux G, et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. *Critical Care Medicine*. 2016;44.2:282–90.
34. Cabrini L, et al. Noninvasive ventilation and survival in acute care settings: a comprehensive systematic review and metaanalysis of randomized controlled trials. *Critical Care Medicine*. 2015;43.4:880–8.
35. Hess DR. Noninvasive ventilation for acute respiratory failure. *Respiratory Care*. 2013;58.6:950–72.
36. Kang BJ, et al. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. *Intensive Care Medicine*. 2015;41.4:623–632.
37. Schunemann HJ, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *American Journal of Respiratory and Critical Care Medicine*. 2006;174.5:605–614.

