

Providing evidence-based care to patients in need of respiratory support

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Noninvasive ventilation (NIV) in the form of bi-level positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP) has long been established as a first-line therapy option for many patients in acute respiratory failure.¹ The goals of providing NIV are to minimize the respiratory workload of the patient in respiratory failure, with the physiologic aim of improving ventilation and oxygenation.

High-flow nasal cannula (HFNC) therapy has been used in adult patients for a number of years, but has gained significant popularity after the Clinical Effect of the Association of Non-invasive Ventilation and High Flow Nasal Oxygen Therapy in Resuscitation of Patients with Acute Lung Injury (FLORALI) study was published in 2015 in the *New England Journal of Medicine*.² In the FLORALI trial, HFNC resulted in lower intubation rates and mortality in patients with *de novo* respiratory failure with $\text{PaO}_2/\text{FiO}_2 < 200$ mm Hg when compared to conventional oxygen therapy (COT) and NIV. Recently, there has been a significant amount of research published regarding the use of HFNC for a wide range of patient populations.³⁻⁵

This article will provide an overview of the current guidelines for NIV and discuss the potential role for HFNC, based on the available data where HFNC has been compared to NIV.

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Acute respiratory failure

Acute respiratory failure (ARF) occurs when a patient no longer has the ability to maintain effective gas exchange. It can be secondary to an imbalance in respiratory drive (i.e., drug-induced, head injury), a decrease in pulmonary perfusion (i.e., increased alveolar dead-space), intra-cardiac or intrapulmonary shunting, or neuromuscular weakness. Studies often look at respiratory rate and oxygenation, and may include arterial pH or PaCO₂ for objective study inclusion criteria for ARF.

Supplemental oxygen and NIV provide the support many patients need to prevent complete respiratory failure (requiring invasive mechanical ventilation). It is important to understand the current evidence regarding the support of patients in respiratory failure, as well as recognize signs of intolerance and failure of these therapies, so that escalation of respiratory support is not delayed.

Evidence-based practice of noninvasive respiratory support

Recently, the European Respiratory Society (ERS), in partnership with the American Thoracic Society (ATS), published updated clinical practice guidelines for NIV.⁶ Many of the recommendations were consistent with previous NIV guidelines published in 2011.¹ The methodology used for these guidelines was created based on the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology to assess the certainty of the evidence. The strength of the recommendation is accompanied by a certainty of effect which evaluates the quality of the evidence for which recommendations are based. The following section will summarize the recommendations and offer insight into the level of certainty of effect provided.

Strong recommendations for NIV continue to be for the management of acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and for acute cardiogenic pulmonary edema (ACPE). For AECOPD, the strong recommendation comes with high certainty in the evidence, which means that further evidence is very unlikely to change the recommendation. For ACPE, the strong recommendation comes with a moderate certainty in the evidence, which means if future studies were performed, it could increase the estimate of effect, or may change the estimate. Currently, there is no evidence that another form of respiratory support used as first-line therapy is as effective as NIV for the management of AECOPD and ACPE.

Conditional recommendations are made when low to moderate evidence exists supporting the effectiveness of a therapy for a specified condition. Many of the conditional recommendations for NIV from earlier studies remain conditional due to inconsistent or weak evidence demonstrating effectiveness for preventing intubation, or reintubation (often the primary outcome measured in studies of NIV), or for demonstrating mortality benefit (normally a secondary outcome measured). Conditional recommendations supporting NIV include managing acute respiratory failure in the following patient conditions: immunocompromised, postoperative, post-extubation (high-risk; prophylaxis), trauma, palliative care, and weaning hypercapnic patients.

No recommendations were made for the management of asthma exacerbation, pandemic viral illness, or *de novo* respiratory failure. *De novo* respiratory failure refers to respiratory failure associated with tachypnea and hypoxemia, in the absence of underlying chronic respiratory disease and acute cardiogenic pulmonary edema. The lack of recommendation is based

on a large amount of data evaluating the use of NIV against COT in acute hypoxemic respiratory failure. Studies have varying degrees of success, some with positive NIV results, others with high NIV failure rates. Unfortunately, NIV failure is associated with poor outcomes.^{7,8} Severity of illness, underlying presence of shock, and level of baseline hypoxemia are predictors of failure of NIV, and extremely close monitoring is important when treating these patients noninvasively. Intubating a patient in hypoxemic failure should not be delayed when there is no clinical signs of improvement.

There were only two **recommendations against** the use of NIV. The use of NIV in AECOPD patients with pH > 7.35 is not recommended as a way of preventing acidosis, and the use of NIV as rescue in patients failing extubation after invasive ventilation is also not recommended.

The role of HFNC in the management of acute respiratory failure

The use of HFNC in the management of acute respiratory failure is rapidly increasing, and studies are regularly being published on the subject. Many studies compare HFNC to either COT or NIV, or both. It is worth noting that most of the evidence in support of HFNC is currently only in the area where conditional or no recommendations are given for the use of NIV. Individual studies have demonstrated benefits over NIV in patients that are immunocompromised and patients in hypoxemic failure (with pH > 7.35). Other studies looking at HFNC used immediately after extubation (transition from invasive ventilation after passing a spontaneous breathing trial) have shown HFNC to be superior over COT in low-risk patients

(low risk of reintubation), and HFNC was non-inferior to NIV immediately after extubation in high-risk patients. There are several systematic reviews and meta-analyses that have looked at the current evidence regarding HFNC and compared it to COT and NIV in mostly hypoxemic respiratory failure. They appear to support the idea that HFNC is superior to COT, but not to NIV.⁹⁻¹³ However, a considerable amount of heterogeneity exists between studies, making the analysis of true effect weak, and further evidence is likely to change the estimate of effect.

When providing support to patients, many clinicians will opt to choose the least invasive option. Although further data is needed to demonstrate a benefit over NIV, it appears that HFNC is a safe alternative for hypoxemic respiratory failure, immunocompromised patients, and immediately post-extubation in patients at low or high risk of extubation failure. However, if hypercarbia occurs during a SBT, or a patient is morbidly obese, NIV should be the preferred therapy post-extubation. Furthermore, unlike NIV, there are currently no clinical guidelines available that are endorsed by groups such as the ERS/ATS. Clinicians should remain aware of the current evidence and understand when it is appropriate to escalate therapy, as was seen in a recent non-inferiority study where noninvasive positive-pressure ventilation (NPPV) prevented intubation in 87% of patients who failed HFT and were subsequently placed on NIV.¹⁴

The clinical conundrum

Depending upon the disease type and clinical presentation of the acute respiratory failure patient, clinicians may choose to treat patients with NIV and HFNC therapy in combination as a means to escalate or de-escalate (wean) quickly. For example, some patients initially treated with HFNC may need rapid escalation to NIV to prevent further escalation to intubation. Others may tolerate intermittent breaks from

NIV and switch to HFNC. However, in all cases, clinicians should be aware of the current evidence and the failure risks associated with both HFNC and NIV, and be ready to quickly escalate therapy to prevent further deterioration or delay of intubation.

Executive summary of the current landscape

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

- Highly recommended
- Recommended
- Mixed evidence
- Inferior
- No data
- High risk

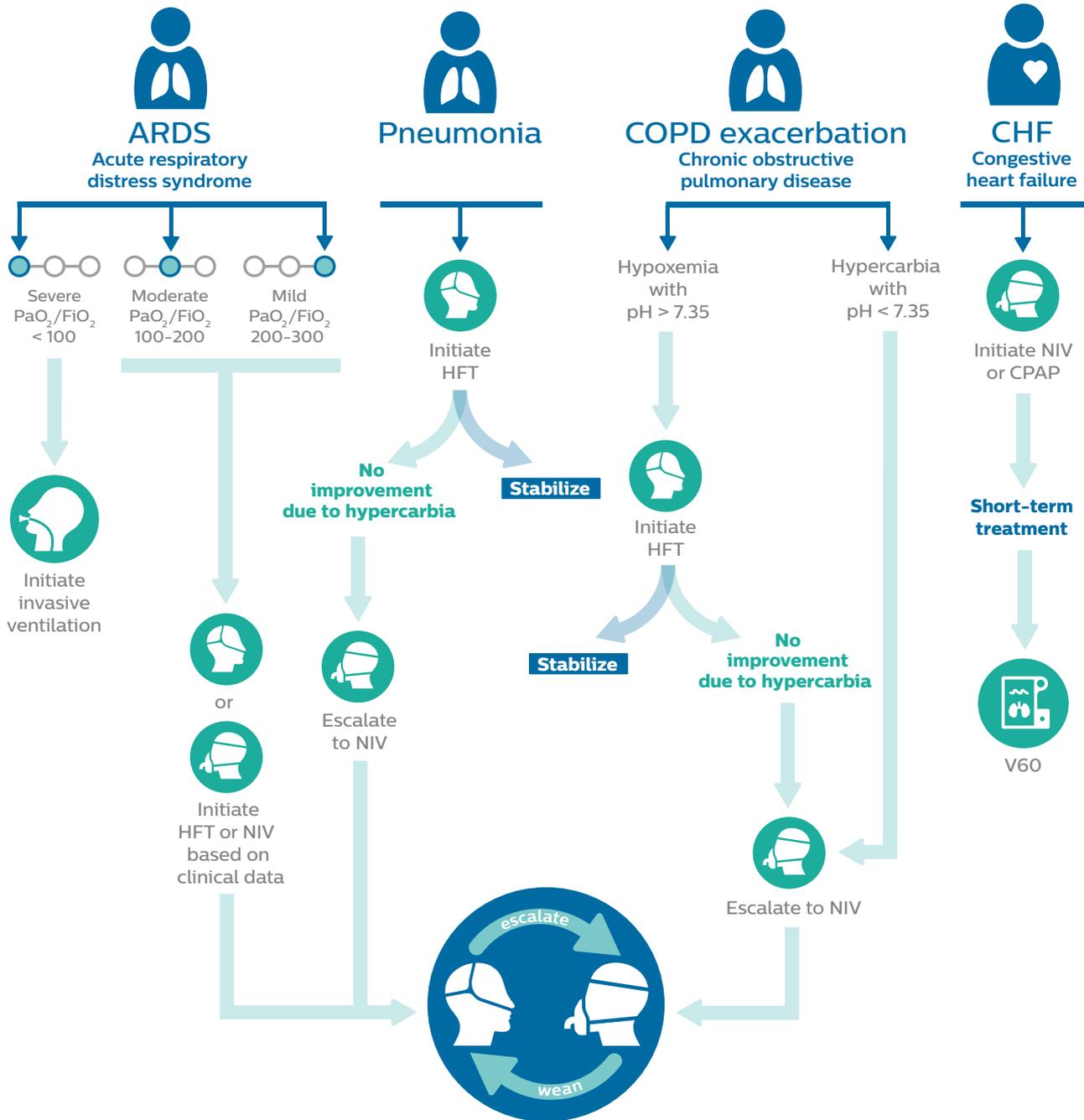
Recommendation based on the author's review of the currently available literature, including existing guidelines.

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

Acute respiratory failure

Work of breathing |
 SpO₂ |
 Heart rate

Diagnosis or condition



These indications likely to use both NIV and HFT

Reference: Rochweg 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. <https://doi.org/10.1183/13993003.02426-2016>.

Conclusion

The use of NIV and HFNC in the management of acute respiratory failure is well supported in the literature. In conditions where there is evidence of efficacy for both HFNC or NIV – such as post-extubation of high-risk patients, mild hypoxemic respiratory failure, immunosuppressed and postoperative patients – the ability of the clinician to rapidly escalate support is important. Having NIV and HFNC available in one

device allows a timely and convenient transition of therapies – whether escalation or de-escalation of therapy – or providing HFNC between NIV sessions. Finally, although the ability to escalate therapy is important, preventing the delay of intubation in patients who need invasive ventilation requires understanding and recognition of predictors of failure.

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