



# Is there still a place for noninvasive ventilation in acute hypoxemic respiratory failure?

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There is **strong evidence** for the use of noninvasive ventilation (NIV) rather than standard oxygen alone to reduce the reintubation rate in several forms of acute respiratory failure (ARF): acute **exacerbation** of chronic obstructive pulmonary disease (COPD), **cardiogenic pulmonary edema**, and **hypoxemia post-abdominal surgery** [1, 2]. The debate lies in the fact that the majority of patients with acute hypoxemic respiratory failure do not fall into these buckets. NIV (with either positive end-expiratory pressure [PEEP] or continuous positive airway pressure) was until recently considered the gold standard of initial oxygenation strategies. A new method of oxygenation was launched in the 2010s, high-flow nasal cannula oxygen (HFNC), providing a high flow of humidified oxygen, with a low level of PEEP (from **2 to 6 cm H<sub>2</sub>O**, depending on the flow rate and the opening or closing of the mouth). The **FLORALI** trial [3] reported in 2015 that **NIV** was independently associated with **increased mortality compared to HFNC** in patients with acute **hypoxemic ARF**. Similar results were observed in the **LUNG SAFE** multicenter observational study by Bellani et al. [4]. However, in the large cohort study by Demoule et al. [5] investigating trends in NIV use over time, NIV failure in acute hypoxemic ARF was no longer associated with mortality in 2010 and 2011, **contrary** to the findings of 1997 and 2002.

In the specific population of ARF immunocompromised patients, a post hoc analysis of the FLORALI trial

confirmed the findings of the initial study, i.e., a **decrease in the mortality rate using HFNC compared to NIV** [6]. However, these **results differed** from those of a dedicated randomized controlled trial (RCT) [7] and a large prospective multinational cohort that reported **no benefit and no harm** from NIV in immunocompromised patients [8].

Some explanations can be proffered when analyzing the better outcome with HFNC compared to NIV. Potential beneficial effects of HFNC include administration of warm and humidified oxygen, providing of a moderate level of PEEP, allowing **less inspiratory effort**, and improved lung volume and compliance. Interface selection may be a major determinant of NIV failure [9]. NIV with a **helmet**, compared with a traditional face mask, was associated with **reduced hospital mortality** and intubation requirement in a single-center randomized study [10]. Regardless of the interface used, **NIV cannot avoid high tidal volumes** when being delivered to hypoxemic patients with **high respiratory drives**, and therefore, possible ventilator-induced lung injury and worsening of respiratory status may occur [11]. It is worth noting that **high tidal volumes might also occur with HFNC**. Table 1 presents the arguments for consideration in favor and against NIV use in hypoxemic ARF patients. In the case of associated decompensation of COPD, fluid overload, or **chest trauma** [12], or in a postoperative setting following abdominal surgery [1], **NIV could** be attempted. In the case of rapid clinical and biological improvement, NIV may be continued until resolution of symptoms. The aim should be **rapid (in 1 h) improvement** in clinical (signs of respiratory **distress**) and biological (**hypercapnia** and **hypoxia**) symptoms. Otherwise, **intubation for invasive mechanical ventilation must be performed**. Dyspnea

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**Table 1 Benefit–risk ratio assessment in favor or against NIV use in hypoxemic ARF patients**

Indications for NIV use
Acute exacerbation of COPD
Acute cardiogenic pulmonary edema
Hypoxemia post-abdominal surgery
Chest trauma
Preoxygenation before intubation
Against NIV use
(Late or moderate–severe) ARDS
High tidal volumes during the NIV session
Leaks during the NIV session despite changes of interface
Lack of patient adherence
Dyspnea during NIV sessions
Impossibility of close monitoring
Absence of rapid clinical improvement (signs of respiratory distress including elevated respiratory rate) and gas exchange improvement after 1 h of NIV session

ARF acute respiratory failure, NIV noninvasive ventilation, COPD chronic obstructive pulmonary disease, ARDS acute respiratory distress syndrome

occurrence during the NIV session is associated with NIV failure when present [13], and may be an important variable to assess when deciding whether to perform an intubation procedure. If **intubation** is deemed appropriate, although apneic oxygenation is the most commonly investigated respiratory support technique for critically ill patients undergoing intubation, **NIV is still the reference method for preoxygenation** of patients with severe hypoxemia [14]. Compared to traditional preoxygenation with an oxygen facial mask during the intubation procedure, NIV for preoxygenation of patients with severe hypoxemic ARF is associated with less hypoxemia [14]. Indeed, combining pressure support with PEEP limits alveolar collapse and atelectasis formation, responsible for hypoventilation and low perfusion ventilation ratio. Using **HFNC combined with NIV** may have advantages over conventional NIV alone for preoxygenation before intubation procedures in hypoxemic patients in the intensive care unit (ICU). The technique of preoxygenation combining NIV and **HFNC—combining** the concepts of **prevention of alveolar derecruitment and apneic oxygenation**, respectively—was recently assessed [15]. Compared with NIV alone, when the combination of NIV and HFNC (OPTINIV method) was used, the lowest saturation during the intubation procedure was significantly increased.

The **literature** is therefore **inconclusive** in terms of **harm or benefit from NIV in hypoxemic ARF** patients. More than the use of NIV, it is the need for invasive mechanical ventilation after NIV failure that

is associated with mortality [5]. However, mortality associated with invasive mechanical ventilation has decreased significantly over the last two decades. Being intubated for mechanical ventilation is not the big bad wolf anymore. The **recent evidence is in favor of not using NIV in ARF** patients (in particular in the case of ARDS), except for those with acute exacerbation of COPD or acute cardiogenic pulmonary edema, or following abdominal surgery or chest trauma. Outside of the peri-intubation period, the use of NIV should best be avoided—at least outside of expert hands and without close monitoring including respiratory rate and **prompt intubation in the case of non-improvement**.

Whatever the method of oxygenation used, the dangers in delaying intubation must be underscored. Indeed, when intubation is delayed in ICU patients, mortality is consistently increased. **One of the first studies showing the risks of a delayed intubation was that of Esteban et al. [16]**. The interval between the onset of respiratory failure and reintubation was significantly longer in the **NIV** group than in the standard-therapy group. Similar results were found with the use of **HFNC [17]**. Kang et al. [17] showed that failure of HFNC might cause delayed intubation and worse clinical outcomes in patients with respiratory failure. Inappropriate use of one of the available oxygen devices (standard oxygen, HFNC, or NIV) might delay intubation and lead to adverse outcomes.

One strategy may not fit all. Individualized patient management would seem to be critical, taking into account the complexity of a single patient. Oxygenation is not the only treatment for hypoxemic ARF. The cause of ARF must be identified and cured, and then the respiratory state of the patient will be able to improve.

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#### Compliance with ethical standards

#### Conflicts of interest

A. De Jong reports personal fees from Baxter and Medtronic-Covidien, and travel reimbursement from Fresenius Kabi, MSD France, Astellas, Pfizer, and Fisher & Paykel. G. Hernandez reports personal fees and travel expenses from Fisher Paykel. D. Chiumello has no conflict of interest.

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