

## ICU Volume 15 - Issue 1 - 2015 - Cover Story - The Lung

### Noninvasive Ventilation



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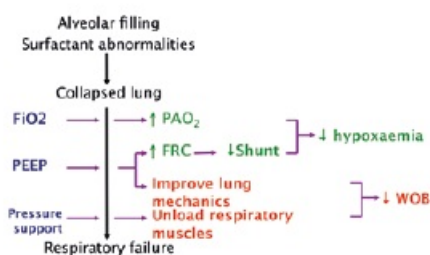
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In less than two decades noninvasive mechanical ventilation (NIV) has become a cornerstone therapy of acute respiratory failure (ARF). It is now well established that NIV can reduce intubation and mortality rates in patients with acute-on-chronic respiratory failure (i.e. severe acute exacerbation of chronic obstructive pulmonary disease) (Brochard et al. 1995) or acute cardiogenic pulmonary oedema (Masip et al. 2000). However, the beneficial effects of NIV remain unclear in patients with de novo acute hypoxaemic respiratory failure, that is nonhypercapnic patients having acute respiratory failure in the absence of a cardiac origin or underlying chronic pulmonary disease. This is all the more true in acute respiratory distress syndrome (ARDS), the most severe form of de novo acute hypoxaemic respiratory failure.

#### Physiologic Rationale for NIV in ARDS

In ARDS inflammation within the alveoli and surfactant abnormalities lead to a lung collapse, which in turn causes a major right-to-left intrapulmonary shunt and a dramatic decrease of lung compliance. This intrapulmonary shunt is responsible for hypoxaemia, while the alteration of lung mechanics increases the work of breathing.



**Figure 1.** Physiopathologic Rationale for NIV Use in Acute Respiratory Distress Syndrome (ARDS).

Figure 1 summarises the physiological impact of NIV in ARDS. The application of positive airway pressure opens collapsed alveoli and increases functional residual capacity, thus decreasing right-to-left intrapulmonary shunt, which in turn leads to a major improvement of hypoxaemia (Katz and Marks 1985). The increase of functional residual capacity improves lung mechanics and thus reduces respiratory load. In combination with the inspiratory unloading that provides positive inspiratory pressure, NIV reduces the work of breathing (L'Her et al. 2005). Together these improvements of hypoxaemia, lung mechanics and respiratory muscle loading are associated with a reduction of dyspnoea (L'Her et al. 2005).

#### Results of Main Studies and Meta-Analyses

To date only five randomised controlled studies have been conducted in patients with de novo hypoxaemic ARF (Confalonieri et al. 1999; Antonelli et al. 2000; Delclaux et al. 2000; Martin et al. 2000; Ferrer et al. 2003). Two of these included hypercapnic patients (Confalonieri et al. 1999; Martin et al. 2000), and one was performed on immunocompromised patients (Antonelli et al. 2000). Only two randomised controlled studies evaluated NIV in non-hypercapnic and immunocompetent patients with de novo ARF. One suggested that NIV may reduce intubation rate and even mortality in a very select population of patients (Ferrer et al. 2003), and the other reported no beneficial effects of continuous positive-end expiratory pressure (Delclaux et al. 2000).

A meta-analysis that included studies on NIV in de novo ARF concluded that, once immunocompromised and hypercapnic patients were removed, the benefit of NIV to prevent intubations was modest, and there was no benefit of NIV on mortality (Keenan et al. 2003). Another meta-analysis focused on the three randomised controlled studies that evaluated the impact of NIV in ARDS (Antonelli et al. 2000; Delclaux et al. 2000; Ferrer et al. 2003). This metaanalysis, that was limited by its sample size, suggested that the addition of NIV to standard care in patients with ARDS did not reduce the intubation rate or ICU mortality (Agarwal et al. 2006).

Despite the lack of evidence for benefit of NIV in de novo hypoxaemic ARF, recent surveys show that NIV is increasingly used in these patients. NIV is initiated as first-line ventilatory support in 10% to 30% of such patients (Demoule et al. 2006; Esteban et al. 2008; Schettino et al. 2008). In ARDS patients a recent proportion meta-analysis of studies that evaluated NIV used as first-line ventilator support showed an overall success rate of 48% (from 30% to 86%) and mortality of 35% (from 15% to 71%) (Agarwal et al. 2010). However, this success rate was much higher in mild ARDS (66%) than in moderate or severe ARDS (32%) (Thille et al. 2013). As a consequence, survival without intubation was also much higher in mild ARDS than in moderate or severe ARDS (Thille et al. 2013).

However, it is important to remain that NIV is more likely to fail in de novo hypoxaemic ARF as compared to acute-on-chronic ARF or acute cardiogenic pulmonary oedema (Demoule et al. 2006).

### What is the Risk of Using NIV in ARDS Patients?

Large cohort studies have demonstrated that NIV is globally beneficial in acute-on-chronic ARF and acute cardiogenic pulmonary oedema (Demoule et al. 2006; Schnell et al. 2014). In addition NIV failure is not a predictor of mortality in these causes of ARF (Demoule et al. 2006). By contrast, NIV failure is an independent predictor of higher hospital mortality in de novo acute respiratory failure. In other words, in de novo acute respiratory failure, NIV failure is associated with a higher mortality regardless of the severity of ARF (Demoule et al. 2006) (see Figure 2). Finally, cohort studies have observed that, in patients with de novo acute respiratory failure, the use of first-line NIV is not associated with better survival (Demoule et al. 2006; Schnell et al. 2014).

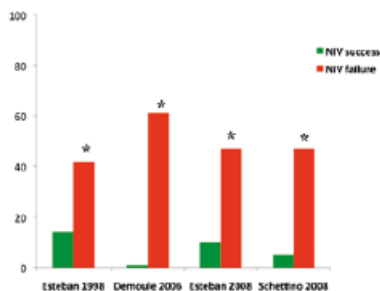


Figure 2. Impact of NIV Success or Failure on Mortality Rate Observed in Surveys.

The reasons why NIV failure is a risk factor for death in de novo hypoxaemic respiratory failure remain unclear. First, intubation may be delayed and therefore performed at the last moment and in catastrophic conditions rather than in early, good conditions. Second, a high level of pressure support in combination with deep inspiratory efforts generates a high level of transpulmonary pressure, which could cause ventilator-induced lung injury.

### Can we Predict NIV Failure in ARDS?

Because NIV failure is associated with a higher mortality in de novo hypoxaemic ARF, it would be interesting to predict early NIV failure and to therefore avoid a delayed intubation. For that purpose, risk factors that would allow the early prediction of NIV failure are of great interest.

A first and major risk factor for NIV failure is the severity of the respiratory failure. Indeed in ARDS patients the success rate of NIV is much higher in mild ARDS (66%) than in moderate or severe ARDS (32%) (Thille et al. 2013).

A second crucial factor is the addition of an extra respiratory failure to ARF. For instance, an altered level of consciousness defined by a low Glasgow Coma Score is an independent predictor of NIV failure in ARDS patients (Thille et al. 2013). Shock is also a clear risk factor for NIV failure and subsequent intubation in ARDS patients (Rana et al. 2006; Carrillo et al. 2012; Thille et al. 2013).

Finally, the response to NIV after two hours provides interesting information regarding the future success or failure of NIV. Indeed a prompt improvement of oxygenation is a good predictor of NIV success (Antonelli et al. 2007). By contrast, a poor tolerance, a high level of leaks or a full dependence on NIV are clear risk factors for NIV failure (Demoule et al. 2006).

### NIV in ARDS Patients: Let's be Practical

The few studies devoted to NIV in ARDS suggest that NIV should only be used in mild ARDS and should not be instituted in case of extra respiratory organ failure. Indeed NIV should not be started in case of an abnormal level of consciousness, severe sepsis or in any case of shock.

In the case of mild ARDS with no extra respiratory failure, NIV can be started, but its tolerance and the response of the patient to NIV should be monitored closely. If tolerance is poor, the level of leaks is important, or if the patient becomes dependent on NIV, then NIV should be stopped immediately and intubation performed promptly. Intubation should also be performed if no improvement is noticed after one to two hours of NIV.

In the Berlin definition of ARDS, NIV is a therapeutic option for mild ARDS that in the opinion of the panel still requires confirmation in prospective clinical trials. These trials are now needed.

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