

Noninvasive ventilation for acute respiratory failure due to community-acquired pneumonia: A concise review and update

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ABSTRACT

Strong evidence supports the use of noninvasive ventilation (NIV) in acute respiratory failure (ARF) to prevent endotracheal intubation (ETI) in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD), cardiogenic pulmonary edema, and immunocompromised patients. However, weaker evidence supports NIV used in acute respiratory distress syndrome (ARDS) and ARF due to community-acquired pneumonia (CAP) in immunocompetent patients owing to high rates of treatment failure. In all patients, NIV should be applied under close monitoring for signs of treatment failure and, in such case, ETI should be promptly available. A trained team, at an appropriate location, with careful patient selection and optimal choice of devices can optimize NIV outcome. In this short review we examine past and more recent literature regarding the use of NIV in ARF due to CAP, discussing the application of both continuous positive airway pressure (CPAP) and pressure support ventilation (PSV).

Key words: Community-acquired pneumonia, noninvasive ventilation, severe respiratory failure

INTRODUCTION

The use of noninvasive ventilation (NIV) in acute respiratory failure (ARF) is now extensive, even if, in more severe cases, such as acute respiratory distress syndrome (ARDS), the evidence is mainly linked to small cohort series.^[1] Among the benefits of NIV there is the possibility of avoiding invasive mechanical ventilation (IMV) and associated

morbidity (increased risk of ventilator-associated pneumonia, ventilator-induced lung injury, increased need of sedation, prolonged ventilation, complications of upper airways, and mortality).^[2]

In community-acquired pneumonia (CAP), the most important rationale for using NIV is to overcome an episode of severe respiratory failure avoiding the need of IMV and, if possible, the admission to the intensive care unit (ICU).^[3,4]


However, the evidence regarding use of NIV in CAP is much less strong than the one related to other diseases such as exacerbation of chronic obstructive pulmonary disease (COPD).^[1]

Patients with ARF due to CAP treated with NIV often show poor outcome,^[2,4] particularly when compared to COPD exacerbation and acute cardiogenic pulmonary edema.^[5,6]

The aim of this short review is to examine past and more recent literature regarding the use of NIV for CAP. We will

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discuss the application of both continuous positive airway pressure (CPAP) and pressure support ventilation (PSV).

THE EARLY YEARS

The first study on NIV including only patients with pneumonia was a multicenter randomized controlled trial (RCT) by Confalonieri *et al.*, in 1999 who divided 56 patients with CAP and ARF into two groups: 28 patients were treated with standard medical therapy and 28 with standard medical therapy plus NIV.^[7] This study showed significant benefits of NIV only in the subgroup of patients with associated COPD.^[7-9] Two years later Jolliet *et al.*, published a study on 24 patients with severe CAP and no prior history of chronic lung disease admitted to the ICU. Despite initial improvement in arterial oxygenation and respiratory rate in 22 out of 24 patients, the intubation rate was very high (66%).^[10] Similar results with high rates of NIV failure in patients with pneumonia and severe ARF were reported by different groups in the subsequent years.^[6,12-16] In 2003, Ferrer *et al.*, in a RCT involving 105 patients (54 treated with medical therapy vs 51 with medical therapy plus NIV) reported a significantly lower rate of intubation, mortality, fatal complications, and length of hospital stay in the NIV group.^[11]

We previously referred to the increased risk of pulmonary infections related to IMV compared to NIV. Given these data, different authors described particular benefit from the application of NIV on patients at high risk of pulmonary infection (such as immunocompromised patients) who showed reduced intubation and mortality rate.^[17,18]

Therefore, the evidence from these preliminary data seemed to show that patients with ARF due to pneumonia were less likely to benefit from NIV when compared to other causes of ARF such as COPD exacerbation and cardiogenic pulmonary edema. However, some subgroups of patients seemed to show particular benefit from a NIV trial, including immunocompromised patients and patients with associated COPD.

THE LESSON OF INFLUENZA A/H1N1 PANDEMIC

During the influenza A/H1N1 pandemic in 2009, a large number of patients with severe ARF were managed in the ICUs. Based on the Toronto experience with severe acute respiratory syndrome (SARS), the use of NIV was discouraged because of inhalation risk. This concept was later questioned by Simonds *et al.*, who found that the droplets generated during NIV are unlikely to remain airborne.^[3,19] However, available evidence did not recommend the extensive use of NIV because its inappropriate application could lead to unnecessary intubation delay.^[16,20]

In the published studies, NIV use ranged from 5 to 100% of the cases with a success rate from 23 to 76%.^[20-37] The

most extensive study on influenza A/H1N1 pneumonia, enrolling a total of 685 patients, including 337 subjects with confirmed influenza A/H1N1, showed a NIV success rate of 41 and 67%, respectively.^[22] This was associated with less radiographic extension and no need of vasopressor therapy.^[16,23] Besides, in most studies the avoidance of intubation was associated with significantly fewer infectious complications, mainly sepsis and septic shock, but also catheter-related infections.^[3,36] Surprisingly, Masclans *et al.*, described a similar mortality in patients who failed NIV trial and in those intubated at presentation.^[23]

MORE RECENT ADVANCES: CAN WE PREDICT NIV FAILURE?

Recently a number of authors investigated potential predictors of NIV success and failure [Table 1]. Carron and coworkers evaluated cardiorespiratory parameters potentially predictive of NIV failure. Patients who failed NIV had higher Simplified Acute Physiology Score (SAPS) II, lower arterial pH, lower PaO₂/FiO₂ (partial pressure of arterial oxygen to the fraction of inspired oxygen) ratio at admission, lower postNIV-preNIV deltas of PaO₂/FiO₂ and higher oxygenation index (determined by mean airway pressure × FiO₂ × 100/PaO₂).^[38] PaO₂/FiO₂ and oxygenation index were the parameters that most helped the decision to intubate. A following study prospectively assessed 184 patients with severe ARF: It showed that patients with *de novo* ARF failed NIV more frequently than patients with previous cardiac or respiratory disease (46% of patients with *denovo* ARF vs 26% of patients with cardiac or respiratory disease). Maximum Sequential Organ Failure Assessment (SOFA) score during NIV, worsening chest X-ray infiltrates 24 h after NIV onset, heart rate after 1 h from NIV starting, PaO₂/FiO₂ ratio after

Table 1: Factors predictive of NIV failure

	Factors predictive of NIV failure
Carron M <i>et al.</i> J Crit Care 2010	Post-NIV to pre-NIV deltas of PaO ₂ /FiO ₂ ratio Post-NIV to pre-NIV deltas of oxygenation index
Carrillo A <i>et al.</i> Intensive Care Medicine 2012	Worsening radiologic infiltrate 24 hours after admission Maximum sepsis-related organ failure assessment (SOFA) score Higher heart rate after 1 hour of NIV (compared to pre-NIV) Lower PaO ₂ /FiO ₂ ratio after 1 hour of NIV (compared to pre-NIV) Lower serum bicarbonates after 1 hour of NIV (compared to pre-NIV)
Nicolini A <i>et al.</i> Clin Respir J 2014	Extensive chest X-ray involvement on admission Chest X-ray worsening 24 hours after admission Lower PaO ₂ /FiO ₂ ratio after 1 hour of NIV (compared to pre-NIV) Higher A-aDO ₂ after 1 hour of NIV (compared to pre-NIV)
Murad A <i>et al.</i> J Crit Care 2015	Vasopressor use at 2 hours after NIV initiation

NIV = Non-invasive ventilation; PaO₂/FiO₂ = Partial pressure of arterial oxygen to the fraction of inspired oxygen; A-aDO₂ = Alveolar-arteriolar oxygen gradient

1 h from NIV onset, and serum bicarbonates 1 hour after NIV onset were the variables independently associated with NIV failure.^[39] In patients with *de novo* ARF who failed NIV, the authors observed an increased mortality associated with a longer duration of NIV. The authors concluded that, in presence of predictors of NIV failure, NIV avoidance would potentially minimize mortality.^[39,16] A more recent series of 127 patients with severe CAP and ARF treated from the beginning with NIV has reported a 25% failure rate. Parameters associated with less severe underlying illness (lower SAPS II and serum lactate dehydrogenase (LDH), limited chest X-ray involvement, higher $\text{PaO}_2/\text{FiO}_2$, and alveolar-arterial oxygen concentration gradient (A-aDO₂) at admission) were predictors of NIV success.^[16,40] In 2015 a retrospective cohort study including 209 critically-ill patients with ARF due to CAP reported an initial NIV trial in 56% of subjects. Of those, 76% failed NIV, though clinical characteristics at onset suggested a more favorable prognosis. Higher Acute Physiology and Chronic Health Evaluation (APACHE) II score at admission and need of vasopressor use within 2 h after initiation of NIV were strictly related to NIV failure.^[41]

Recently, some prospective studies reported good outcomes related to the use of NIV in patients with CAP.^[42-44] A wide retrospective cohort study on immunocompromised patients hospitalized with pneumonia (1,946 patients - 717 received NIV) described a beneficial association between the use of NIV and mortality: NIV use was associated with lower 30- and 90-day mortality compared to IMV.^[43] Finally, two RCTs recently published demonstrated the usefulness of NIV in ARF due to CAP: The authors showed that the use of helmet CPAP 10 cmH₂O rapidly improved gas exchange and reduced the risk of meeting endotracheal intubation (ETI) criteria compared to oxygen therapy alone.^[44,45]

Therefore, an accurate and prompt evaluation of factors that can predict NIV success or failure may help to select those that are most likely to respond to NIV and may avoid delay in ETI.

WHAT HAVE WE LEARNED?

Risom *et al.*, in a retrospective study showed that NIV is less efficient in pneumonia than in COPD exacerbation (NIV failure rate 5% in COPD exacerbation vs 49% in CAP, $P < 0.0001$; and in-hospital mortality 14% in COPD exacerbation vs 21% in CAP, $P < 0.01$).^[5] Although the main reason for choosing NIV in patients with severe ARF due to CAP is to avoid the complications associated with IMV, clinicians should carefully consider elements that may predict NIV failure, thus preventing dangerous delay in ETI [Figure 1].^[46-48] Patients with CAP and severe ARF evolving into ARDS (acute onset, bilateral infiltrates on chest X-ray, and $\text{PaO}_2/\text{FiO}_2$ ratio <200 according to the new

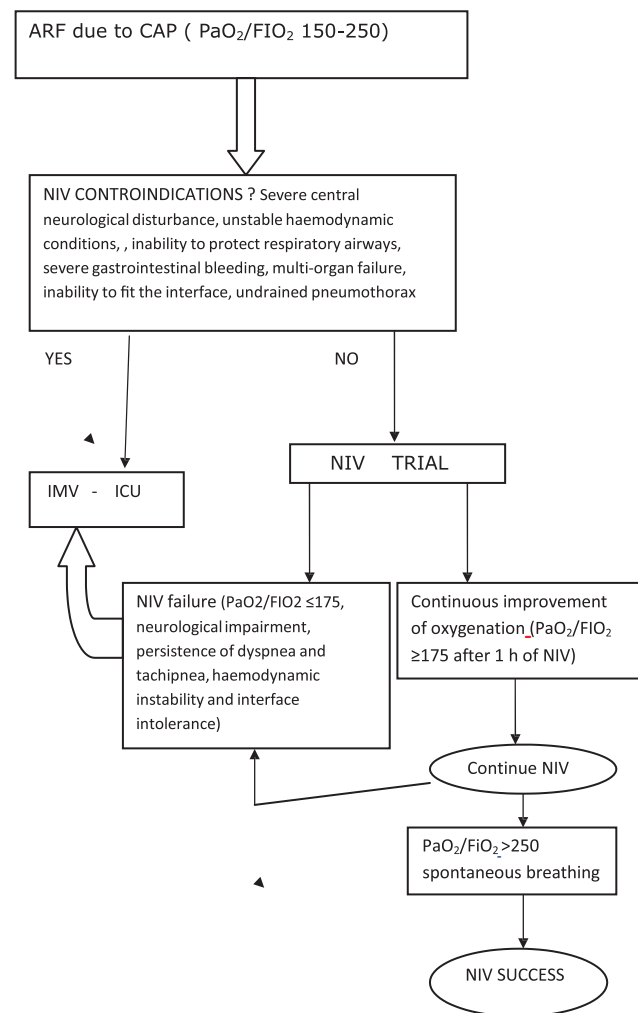


Figure 1: Flow chart to decide NIV appropriateness and success. ARF = Acute respiratory failure, CAP = Community-acquired pneumonia, IMV = Invasive mechanical ventilation, ICU = Intensive care unit, NIV = Noninvasive ventilation

Berlin definition^[46,49]) could safely be treated up to a $\text{PaO}_2/\text{FiO}_2$ ratio as low as 150 using assisted ventilation with a target tidal volume of 6-8 mL/kg and positive end-expiratory pressure (PEEP) of 5-10 cmH₂O.^[20,40,50,51] The ventilator (ventilators specifically designed for NIV to compensate for air leak) and interface choice to optimize patient's comfort and ventilatory efficiency are also considerable points for NIV success.^[3,47,52-54] Location and timing are other two crucial points in determining the success of NIV: These patients need a continuous monitoring to avoid delayed intubation.^[51,55,56] High-dependency respiratory unit could be the ideal environment where to perform NIV.^[57] Finally, medical and nursing staff experience and skills are key components to reach positive outcomes. Specific staff training has shown to reduce nosocomial infections, to improve survival in critically ill patients,^[58] to allow treatment of more severe cases,^[59,60] and to decrease time spent by nurses at patients' bedside.^[10,56]

CONCLUSIONS

Although latest results are promising and NIV can be considered a valuable option to treat severe ARF due to CAP, a cautious approach is advisable, limiting the use of NIV to patients with less severe disease (SAPS II <34, PaO₂/FiO₂ at presentation >150, or PaO₂/FiO₂ after 1 h from NIV onset >175). Close monitoring and management by experienced personnel in order to early detect NIV failure and, thus, avoid ETI delay are two other key points for NIV trial success.

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