

Noninvasive ventilation in acute respiratory failure

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Background: Noninvasive ventilation has assumed an important role in the management of respiratory failure in critical care units, but it must be used selectively depending on the patient's diagnosis and clinical characteristics.

Data: We review the strong evidence supporting the use of noninvasive ventilation for acute respiratory failure to prevent intubation in patients with chronic obstructive pulmonary disease exacerbations or acute cardiogenic pulmonary edema, and in immunocompromised patients, as well as to facilitate extubation in patients with chronic obstructive pulmonary disease who require initial intubation. Weaker evidence supports consideration of noninvasive ventilation for chronic obstructive pulmonary disease patients with postoperative or postextubation respiratory failure; patients with acute respiratory failure due to asthma

exacerbations, pneumonia, acute lung injury, or acute respiratory distress syndrome; during bronchoscopy; or as a means of preoxygenation before intubation in critically ill patients with severe hypoxemia.

Conclusion: Noninvasive ventilation has assumed an important role in managing patients with acute respiratory failure. Patients should be monitored closely for signs of noninvasive ventilation failure and promptly intubated before a crisis develops. The application of noninvasive ventilation by a trained and experienced intensive care unit team, with careful patient selection, should optimize patient outcomes. (*Crit Care Med* 2007; 35:2402–2407)

KEY WORDS: noninvasive ventilation; acute respiratory failure; intubation prevention

Noninvasive ventilation (NIV), a form of ventilatory support that avoids airway invasion, has seen increasing use in emergency departments and intensive care units (ICUs) in recent years, based on the results of clinical trials showing improved outcomes in certain types of acute respiratory failure (ARF) (1). NIV usually refers to the provision of inspiratory pressure support plus positive end-expiratory pressure (PEEP) via a nasal or face mask. Although continuous positive airway pressure (CPAP) does not actively assist inspiration and is not a ventilatory support mode, it is considered a form of NIV here when used as a therapy for ARF. The successful application of NIV requires the training and collaboration of an experienced ICU team, including intensivists, nurses, and respiratory thera-

pists (2). This review will focus on the evidence supporting the use of NIV in various forms of respiratory failure (Table 1), selection of appropriate patients, and techniques for successful implementation.

NIV FOR SPECIFIC TYPES OF ACUTE RESPIRATORY FAILURE: EVIDENCE AND RECOMMENDATIONS

Hypercapnic Respiratory Failure

Chronic Obstructive Pulmonary Disease. NIV should be considered first-line therapy in the management of ARF caused by chronic obstructive pulmonary disease (COPD) exacerbations based on evidence derived from multiple randomized trials (2–5). Meta-analyses by Dr. Lightowler and colleagues (6) and Dr. Keenan and colleagues (7) show reduced intubation rates, hospital lengths of stay, and mortality with NIV use. The strength of the evidence justifies the application of NIV as a standard of care in appropriately selected patients with hypercapnic ARF due to COPD. Although considered a contraindication to NIV in the past, hypercapnic coma in patients with COPD can be treated with NIV as successfully as in noncomatose patients (8, 9).

The use of NIV as an alternative to endotracheal intubation in more severely

ill patients (i.e., those with a pH <7.2) has been controversial. However, recent studies demonstrate that outcomes of severe COPD exacerbations are no worse if treated with NIV than with endotracheal intubation (10, 11), indicating that an initial trial with NIV is not deleterious, even in severely ill COPD patients.

Asthma. Evidence is weaker for the use of NIV in asthma patients with acute respiratory failure. An uncontrolled study (12) observed improved gas exchange and avoidance of intubation in 15 of 17 patients with status asthmaticus, and all patients survived. A subsequent randomized pilot study in 33 patients with acute asthma but not ARF showed improved flow rates and decreased hospitalizations with NIV vs. sham NIV (13). However, Dr. Ram and colleagues (14) concluded that large randomized controlled trials (RCTs) are needed before recommending NIV use in status asthmaticus. A trial of NIV can be considered in asthmatics who fail to respond adequately to initial bronchodilator therapy to improve air flow obstruction and decrease the work of breathing. Patients should be monitored closely and intubated promptly if there is no improvement in the first hour or two, because these patients can deteriorate rapidly.

Facilitating Extubation in COPD. Facilitation of extubation in patients with ARF due to COPD exacerbations is an

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Table 1. Noninvasive ventilation for various types of acute respiratory failure (ARF): Evidence for efficacy and strength of recommendation

Type of ARF	Level of Evidence ^a	Strength of Recommendation ^b
Hypercapnic respiratory failure		
COPD exacerbation	A	Recommended
Asthma	C	Option
Facilitation of extubation (COPD)	A	Guideline
Hypoxemic respiratory failure		
Cardiogenic pulmonary edema	A	Recommended
Pneumonia	C	Option
ALI/ARDS	C	Option
Immunocompromised	A	Recommended
Postoperative respiratory failure	B	Guideline
Extubation failure	C	Guideline
Do not intubate status	C	Guideline
Preintubation oxygenation	B	Option
Facilitation of bronchoscopy	B	Guideline

COPD, chronic obstructive pulmonary disease; ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

^aA, multiple randomized controlled trials and meta-analyses; B, more than one randomized, controlled trial, case control series, or cohort studies; C, case series or conflicting data; ^b recommended, first choice for ventilatory support in selected patients; Guideline, can be used in appropriate patients but careful monitoring advised; Option, suitable for a very carefully selected and monitored minority of patients.

other application of NIV supported by strong evidence. In intubated patients with COPD and hypercapnic respiratory failure who failed a single (15) or repeated T-piece trials (16) and were extubated to NIV or continued on invasive ventilation and weaned according to a standard pressure support protocol, randomized trials showed an increased weaning rate at 28 days, decreased durations of mechanical ventilation and ICU stay, and reduced rates of nosocomial pneumonia and 60-day mortality. Based on these findings, patients intubated for hypercapnic respiratory failure due to COPD who fail spontaneous breathing trials should be considered for a trial of extubation to NIV. This approach should be reserved for patients who are good candidates for NIV in other respects and who are able to tolerate levels of pressure support easily administered via mask (i.e., ≤ 15 cm H₂O). In addition, they should not have been a difficult intubation.

Hypoxemic Respiratory Failure

Hypoxemic ARF is defined by a PaO₂/FIO₂ ratio < 200 and a variety of different non-COPD etiologies. It is a very broad category, and studies focusing on it are difficult to apply to individual patients. The concern is that responses within an etiologic subcategory—harmful or beneficial—could be obscured by responses in other subcategories. Therefore, the fol-

lowing will consider studies focusing on the subcategories.

Cardiogenic Pulmonary Edema. The use of NIV or CPAP in patients with cardiogenic pulmonary edema is supported by multiple randomized trials (17–23). The main physiologic benefit from NIV or CPAP in these patients is likely due to an increase in functional residual capacity that reopens collapsed alveoli and improves oxygenation. This also increases lung compliance and reduces work of breathing. The increased intrathoracic pressure also can improve cardiac performance by decreasing ventricular preload and afterload.

Several meta-analyses have shown equivalent reductions in intubation and mortality rates with CPAP and NIV for cardiogenic pulmonary edema, although the reduction in mortality with NIV was not statistically significant in some, probably because there were fewer NIV than CPAP studies (24, 25). However, several studies have shown more rapid reductions in respiratory rate and dyspnea with NIV than with CPAP alone (20, 26). Thus, either NIV or CPAP can be used to treat cardiogenic pulmonary edema with equal expectations of success. Some recommend starting with CPAP, because it is a simpler and potentially less expensive therapy, with pressure support added if patients remain dyspneic or hypercapnic on CPAP alone.

Pneumonia. Pneumonia has been a challenge to treat noninvasively and has

been identified as a risk factor for NIV failure (27). Two thirds of patients with severe community-acquired pneumonia required intubation after being started on NIV in one cohort study, even though those who succeeded with NIV had very good outcomes (28). An RCT on patients with severe community-acquired pneumonia showed that NIV reduced intubation rates, ICU length of stay, and 2-month mortality rate, but only in the subgroup with underlying COPD (29). Another RCT on patients with hypoxemic respiratory failure (30) showed that NIV reduced the need for intubation among patients with pneumonia (26% vs. 73% in the conventional therapy group), but a more recent RCT (31) testing NIV as an alternative to invasive ventilation in patients with various types of ARF found that the subgroup with pneumonia did very poorly, with all eight patients randomized to NIV requiring intubation. The scant and conflicting data do not support the routine use of NIV in patients with severe pneumonia, with the exception of patients with underlying COPD. However, a cautious trial of NIV may be considered in patients with pneumonia deemed to be excellent candidates, but they need careful monitoring, because the risk of failure is high.

Acute Lung Injury/Acute Respiratory Distress Syndrome. Studies on NIV to treat acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) have reported failure rates ranging from 50% to $> 80\%$ (27, 30, 32, 33), but no RCTs have focused on ALI/ARDS exclusively. Independent risk factors for NIV failure in this group of patients include severe hypoxemia, shock, and metabolic acidosis (33). A recent prospective multicenter survey found that when NIV was used as first-line therapy for selected ALI/ARDS patients (those with > 2 organ failures, hemodynamic instability, or encephalopathy were excluded), 54% avoided intubation and had excellent outcomes (34). Predictors of NIV failure were Simplified Acute Physiology Score II > 34 and PaO₂/FIO₂ ≤ 175 after the first hour of therapy. Thus, although NIV cannot be recommended as routine therapy for ALI/ARDS, these data support a cautious trial in highly selected patients with a Simplified Acute Physiology Score II ≤ 34 and readiness to promptly intubate if oxygenation fails to improve sufficiently within the first hour.

Respiratory Failure in Immunocompromised Patients. RCTs in recipients of

solid-organ or bone-marrow transplants who developed hypoxemic respiratory failure have found decreased intubation and ICU mortality rates and shorter ICU lengths of stay in patients treated with NIV as compared with conventional therapy (35, 36). Similar findings have been reported for acquired immune deficiency syndrome patients in a nonrandomized study (37). The reduced mortality is likely related to reduced infectious complications associated with NIV use compared with endotracheal intubation, including ventilator-associated pneumonia, other nosocomial infections, and septic shock (38). These data support NIV as the preferred initial ventilatory modality for these patients, to avoid intubation and its associated risks.

Postoperative Respiratory Failure

Both CPAP and NIV have shown benefit in the postoperative period. When used prophylactically after major abdominal surgery (39) or thoracoabdominal aneurysm repair (40), CPAP (10 cm H₂O) reduces the incidence of hypoxemia, pneumonia, atelectasis, and intubations compared with standard treatment. In the only RCT of NIV in the postoperative setting, patients with hypoxemic respiratory failure after lung resection had reduced intubation and mortality rates if treated with NIV when compared with standard management (41). Because these studies have examined different techniques following various surgeries, firm specific recommendations cannot be made. However, the data lend support to the use of CPAP or NIV in postoperative patients, either prophylactically in high-risk patients or as an early therapy of respiratory insufficiency.

Postextubation Respiratory Failure

Extubation failure is associated with high morbidity and mortality, and NIV has been suggested as a way to avoid re-intubation and improve outcomes. An earlier RCT found no reduction in reintubations among patients who developed respiratory distress within 48 hrs of extubation, although few patients with COPD were included in this study and the level of pressure support used may have been subtherapeutic (42). Another RCT attempted to prevent extubation failure by starting NIV (or continuing standard

therapy) as soon as patients developed signs of extubation failure (43). Surprisingly, not only did NIV fail to reduce reintubations, but its use also was associated with increased ICU mortality, thought to be related to delays in needed reintubation. Only 10% of patients in this trial had COPD, however. Two subsequent RCTs (44, 45) on patients deemed to be at high risk for extubation failure found that NIV reduced the need for reintubation and ICU mortality, but in one of the studies the hypercapnic subgroup (mainly COPD patients) had most of the benefit (45). These data support the use of NIV in patients at high risk of extubation failure, particularly if they have COPD, congestive heart failure, and/or hypercapnia. However, early indiscriminate use in all patients with risk factors is discouraged. Patients with extubation failure treated with NIV should be monitored closely and delays in needed intubation avoided.

Palliative Care and Do-Not-Intubate Status

A prospective cohort series (46) evaluated 114 patients with acute respiratory failure and a status of do not intubate. Overall, 43% of the patients survived the hospitalization, and those with diagnoses of cardiogenic pulmonary edema and COPD had hospital survival rates >50%. The presence of a cough and an awake mental status imparted a favorable prognosis. Another prospective cohort series also showed favorable success rates in do not intubate patients with COPD and cardiogenic pulmonary edema, but a high failure rate in patients with hypoxemic respiratory failure, postextubation failure, and end-stage cancer (47). Depending on patient and/or family wishes, a trial of NIV can be considered in do-not-intubate patients, but the goals of therapy should be clear (48). If the patient and/or family desire prolonged survival, then use should be reserved primarily for COPD and congestive heart failure patients. On the other hand, if the goal is to palliate, to relieve dyspnea, or to delay death so that affairs can be settled, then NIV can be used for these as well as other diagnoses. However, it should be reassessed frequently and stopped if the goal of palliation is not being met.

Other ICU Applications of NIV

Preoxygenation Before Intubation. Critically ill patients with hypoxic respi-

ratory failure are at high risk of oxygen desaturations during intubation. A recent RCT of such patients (49) showed that preoxygenation with NIV before intubation resulted in improved oxygen saturation during and after intubation and decreased the incidence of oxygen desaturations below 80% during intubation. This approach is promising but should be further studied before routine use can be recommended.

Fiberoptic Bronchoscopy. A RCT has shown that CPAP alone (up to 7.5 cm H₂O) improves oxygenation and reduces postprocedure respiratory failure in patients with severe hypoxemia undergoing bronchoscopy (50). In an RCT (51) of 26 patients with hypoxemia (PaO₂/FIO₂ ratio <200), NIV increased PaO₂/FIO₂ by 82% compared with a 10% worsening in the conventional oxygen therapy group. Successful bronchoscopy during NIV also has been reported in hypercapnic COPD patients with pneumonia. NIV improved oxygen saturation, and all 10 patients tolerated the procedure without complications (52). The evidence supports the use of NIV during fiberoptic bronchoscopy, especially when risks of intubation are deemed high, such as in immunocompromised patients or in those with bleeding diatheses. However, the ICU team must be prepared for the possibility of emergent intubation.

PATIENT SELECTION

Selection of appropriate patients is an important skill that is key to the successful application of NIV. In brief, it is a clinical judgment that takes into consideration the etiology of the ARF and evidence for efficacy (Table 1). Good candidates for NIV have a demonstrable need for ventilatory assistance and no contraindications to NIV (Table 2). In addition, consideration of predictors of success and failure may be helpful (Table 3); intubation is preferred if the likelihood of failure is too great. Numerous studies have demonstrated that the response to NIV after the first hour or two is the best predictor of eventual outcome (27, 34, 53). Therefore, when in doubt, a brief, cautious trial of NIV can be attempted, with plans to intubate if the patient fails to improve sufficiently.

NIV TECHNIQUES

Although technical aspects such as choice of interface and ventilator settings are clearly important to NIV success, the

Table 2. General guidelines for selection of patients for noninvasive ventilation

1. Need for ventilatory assistance? Moderate to severe dyspnea Tachypnea (>24 for hypercapnic, 30 for hypoxemic) Accessory muscle use Abdominal paradox PaCO ₂ >45 mm Hg, pH <7.35 PaO ₂ /FIO ₂ <200	2. Contraindications for NIV? Respiratory arrest Medically unstable Unable to protect airway Excessive secretions Agitated, uncooperative Recent UGI or airway surgery Unable to fit mask
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NIV, noninvasive ventilation; UGI, upper gastrointestinal.

Table 3. Predictors of failure: Noninvasive ventilation (NIV) for acute respiratory failure^a

<p>COPD Air leaking APACHE II $\geq 29^b$ Asynchrony Copious secretions Glasgow Coma Score $\leq 11^b$ Lack of "compliance" or "tolerance" pH <7.25^b Respiratory rate ≥ 35 breaths/min^b</p> <p>Hypoxemic respiratory failure ALI/ARDS SAPS II ≥ 35 Metabolic acidosis PaO₂/FIO₂ ≤ 146 (or ≤ 175 for ARDS) after 1 hr of NIV Pneumonia Severe hypoxemia Shock</p>

COPD, chronic obstructive pulmonary disease; APACHE II, Acute Physiology and Chronic Health Evaluation II; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; SAPS II, Simplified Acute Physiology Score II.

^aBased on composite from Ambrosino Thorax '94 Confalonieri, Rana, Antonelli ICM 2001, Antonelli CCM 2006; ^b likelihood of failure >50% if any three and 82% if all four present at baseline; >75% if any three and 99% if all four present after 2 hrs of NIV.

human factor is important, as well. As caregivers in one ICU gained experience with NIV, success rates remained stable even as more severely ill patients were treated (54).

Selection of an Interface. Selection of a properly fit and comfortable interface is critical to NIV success. Although patients rate nasal masks as more comfortable than full face masks (55), an RCT demonstrated that full face masks are better tolerated than nasal masks for ARF because of less air leaking through the mouth (56).

Selection of a Ventilator and Ventilator Settings. Either critical care or bilevel positive-pressure ventilators can be used to administer NIV to ARF patients; no study has demonstrated superiority of one type over the other. Although many

Table 4. Monitoring of noninvasive ventilation for acute respiratory failure

<p>Subjective Mask comfort Tolerance of ventilator settings Respiratory distress</p> <p>Physical findings Respiratory rate Other vital signs Accessory muscle use Abdominal paradox</p> <p>Ventilator parameters Air leaking Adequacy of pressure support Adequacy of PEEP Tidal volume (5–7 mL/kg) Patient-ventilator synchrony</p> <p>Gas exchange Continuous oximetry (until stable) ABGs, baseline and 1–2 hrs, then as indicated</p> <p>Location Usually ICU or respiratory care unit to start General ward may be OK if patient stable Depends on monitoring needs of patients and monitoring capabilities of unit</p>
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PEEP, positive end-expiratory pressure; ABGs, arterial blood gases; ICU, intensive care unit.

critical care ventilators now offer NIV modes that provide pressure support ventilation with leak compensation and silencing of nuisance alarms, little data are available to demonstrate clinical efficacy. The determination of optimal ventilator settings also has been inadequately studied, but is usually a process of balancing the ability to reduce work of breathing by providing an adequate level of pressure support (usually >8–10 cm H₂O) against the discomfort and greater air leaking imposed by higher pressures. A common mistake is to start with a low inspiratory pressure to facilitate tolerance and then to fail to titrate pressures upward to reduce respiratory effort.

In COPD, the inspiratory threshold load imposed by intrinsic PEEP is a major component of the work of breathing. External PEEP, usually not higher than 5 cm H₂O to 7 cm H₂O, should be provided with pressure support to these patients to minimize inspiratory effort (57).

In a study designed to determine optimal NIV settings in patients with ALI, a PEEP of 10 cm H₂O improved PaO₂/FIO₂ more than a PEEP of 5 cm H₂O (58). A pressure support of 15 cm H₂O and a PEEP of 5 cm H₂O decreased PaCO₂, respiratory rate, and work of breathing, and improved dyspnea more than a pressure support of 10 cm H₂O and PEEP of 10 cm H₂O, even though PaO₂/FIO₂ was better with the higher PEEP. This study shows that adjusting settings may require a balancing of beneficial and adverse effects to come up with the best combination for a given patient.

Monitoring of NIV. To assure the success of NIV, close monitoring is necessary, especially during the initiation period (Table 4). Favorable subjective responses—including tolerance of the mask and air pressure and reduction of respiratory distress and effort—are important to establish early. Air leaking should be sought and minimized, and gas exchange should be stabilized and improved.

The location of NIV delivery also is important to assure adequate monitoring. Most studies have monitored patients in ICUs or respiratory step-down units, but some have reported successful application of NIV on general medical wards (59, 60). Monitoring should be tailored to the acuity of illness. If the patient becomes unstable within minutes of mask removal, then close monitoring is mandatory, ideally in an ICU or respiratory unit.

CONCLUSION

Strong evidence from randomized trials supports the use of NIV in the management of ARF to prevent endotracheal intubation in patients with COPD exacerbations or acute cardiogenic pulmonary edema, and in immunocompromised patients, as well as to facilitate extubation in patients with COPD. NIV should be contemplated in patients with postoperative respiratory failure or at high risk for postextubation respiratory failure who are otherwise good candidates for NIV, and as a means of preoxygenating critically ill patients with hypoxemia before intubation. NIV can be considered in patients with asthma exacerbations, pneumonia, and ALI/ARDS, although the supporting evidence is fairly weak; these and other acutely ill patients should be monitored closely for signs of NIV failure until stabilized. If there are signs of NIV fail-

ure, patients should be intubated promptly before a crisis develops. The application of NIV by a trained and experienced ICU team, with careful patient selection, should optimize patient outcomes.

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