
Acute Respiratory Failure: NIV Implementation and Intubation

5

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Case Presentation

A 65 year-old woman with a history of ischemic cardiomyopathy and thromboembolic stroke presented with dyspnea, tachypnea (respiratory rate 36 breaths/minute), cough, fever, and oxygen desaturation to 85 % despite non-rebreather mask at 10 L/min. During her initial resuscitation she was treated with noninvasive ventilation via bilevel positive airway pressure (BPAP) ventilation. Thirty minutes later, the patient's oxygen saturation had steadily improved to 94 % on FiO₂ of 0.7, and her respiratory rate had decreased to 28, though she remained febrile. Initial diagnostics revealed a white blood cell count of 19,500. The chest x-ray is shown below in Fig. 5.1.

Question What is the next appropriate step in the management of this patient?

Answer Depending on her goals of care, this patient should most likely be intubated and undergo invasive ventilation.

While non-invasive ventilation has been shown to be effective and safe in patients with exacerbations of COPD and CHF, other conditions are more controversial. The use of NIV in patients with pneumonia who progress to acute respiratory failure has been associated with a high failure rate and rapid deterioration, leading to worse outcomes, including increased mortality. Both NIV (Fig. 5.2) and the use of high-flow, heated, humidified oxygen delivered by nasal cannula (Fig. 5.3) (see section “Evidence Contour”) may improve respiratory and gas exchange parameters, but it is challenging to predict which patients will definitively improve with this strategy. Individualized care and continuous bedside reassessment are essential. In this case, the patient was emergently intubated and treated with broad-spectrum antibiotics prior to ICU admission. After 4 days, she was successfully extubated and transferred to the general medical ward, where she continued to improve prior to discharge on oral antibiotics.

Principles of Management

Definition

Acute respiratory failure manifests as hypoxemia and/or hypoventilation, which can lead to global ischemia and acid/base disturbances. Depending on patient factors and the type of respiratory failure, patients generally require some degree of respiratory support, ranging

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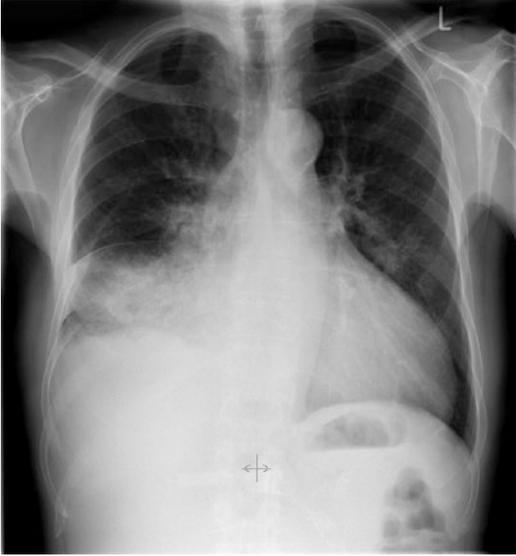


Fig. 5.1 Chest x-ray

from supplemental oxygen via nasal cannula to high-flow oxygen therapy, non-invasive ventilation, and invasive ventilation. High-flow oxygen therapy can be delivered via face mask or high flow nasal cannula (Fig. 5.3). The term non-invasive ventilation (NIV) encompasses all forms of mechanically assisted ventilation without an artificial airway in place. NIV refers to both negative pressure ventilation (no longer used in clinical practice) and positive pressure ventilation modes, which include continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BPAP) ventilation. Both are typically delivered via a tightly-fitting mask, which can be fitted over the nose, nose and mouth, face, or entire head. CPAP delivers various air/oxygen ratios at a constant pressure throughout both inspiration and expiration, which can improve alveolar recruitment and capillary oxygen delivery. BPAP provides both this continuous level of baseline expiratory positive airway pressure (EPEP) and then a higher level during inspiration (IPAP). Depending on the settings, cycling between these two pressure levels is triggered by the patient and/or a pre-set rate chosen by the clinician.



Fig. 5.2 Non-invasive ventilation by full face mask



Fig. 5.3 Hi-flow nasal cannula

The theoretical benefit of BPAP over CPAP is this additional pressure support during inspiration, which can augment the patient's tidal volume and reduce the mechanical work of breathing [1]. Because of their impact on intrathoracic pressure, both of these modes of NIV can also have hemodynamic effects, including both preload and afterload reduction. Depending on the patient and pathology, these effects can offer additional therapeutic benefit, but can also exacerbate hemodynamic compromise.

Indications, Contraindications and Settings

The most widely accepted indications for the use of NIV in the acute setting include respiratory failure due to acute decompensated heart failure (ADHF) and acute exacerbations of chronic obstructive pulmonary disease (COPD). Early use of NIV is associated with improved survival in patients with these conditions [2, 3]. Common chronic indications include obstructive sleep apnea and restrictive diseases of the chest wall, such as muscular dystrophies and obesity hypoventilation syndrome. In order for NIV to be safe and effective, patients' mental status must not be altered to the point where they will not cooperate with the clinician or tolerate the face mask, nor should they have impaired inability to protect their airway from excessive secretions or emesis. Specifically, this includes all unresponsive and apneic patients, in whom intubation and invasive ventilation is the only reasonable mode of ventilatory support. Certain craniofacial abnormalities may also prevent an effective mask seal.

Patients with ADHF develop respiratory failure due in part to the presence of pulmonary edema [1]. CPAP is commonly used in these patients, as it can provide rapid preload and afterload reduction and augment alveolar recruitment, improving oxygenation and minimizing ongoing coronary ischemia [4]. CPAP is often initially set at 5 cm H₂O and titrated to a

combination of patient tolerance and clinical effect. If they tolerate the mask, patients often describe an initial subjective improvement in their work of breathing. Objective clinical improvement, such as the resolution of pulmonary rales and jugular venous distension, usually lags somewhat behind.

BPAP can be a particularly helpful mode in patients with impaired gas exchange secondary to respiratory muscle fatigue, as commonly seen in patients with acute exacerbations of COPD. Beyond the alveolar recruitment conferred by the baseline EPAP, the addition of pressure support during inspiration can provide a mechanical advantage and thus further decrease the work of breathing, which otherwise consumes a tremendous amount of metabolic energy. Additional IPAP also creates more effective airway ventilation and CO₂ removal. Typical initial BPAP settings are an EPAP of 5 cm H₂O and an IPAP of 10 cm H₂O. In response to persistent respiratory acidosis, IPAP may be increased (usually in increments of 2 cm H₂O). This increases the difference between EPAP and IPAP, which is the primary contributor to augmented ventilation. In response to persistent hypoxemia, EPAP may also be increased in increments of 2 cm H₂O. This is most likely to augment alveolar recruitment and oxygenation. Clinicians should be mindful that the pressure required to overcome the tone of the lower esophageal sphincter is approximately 20–22 cm H₂O. Keeping the IPAP below this level may reduce the risk of accidental gastric insufflation, vomiting, and possible aspiration.

Predictors of Failure of Non-invasive Ventilation

It is important to recognize when a patient may not improve with NIV. Very limited evidence is available to guide decision-making in these patients. In a 2003 prospective cohort study of severe dyspnea due to decompensated heart failure, Giacomini and colleagues derived a crude

protocol that addresses the transition from the emergency department to inpatient care for patients stabilized with NIV. After a 90-min trial of NIV, patients who felt subjectively better and tolerated at least a 15-min period of oxygen by reservoir mask were admitted to a general care ward. None of these “responder” patients were subsequently intubated or transferred to ICU [5]. Patients who remained tachypneic, acidemic, or hypoxemic after a trial of NIV (60–90 min), and those who developed hypotension, were unlike to improve. For these “non-responder” patients, endotracheal intubation and invasive ventilation should be strongly considered, as the role of prolonged acute treatment with NIV is still unclear.

Strong evidence outlining safe titration of NIV in other patient subgroups is lacking. Factors to consider include patient comorbidities and physiologic reserve, as well as the expected time course of reversibility for the cause of their acute respiratory failure.

Evidence Contour

Use in Patients with Pneumonia

The use of NIV in acute respiratory failure has been studied for indications other than decompensated heart failure and COPD [6–10]. Pneumonia is not considered an appropriate indication for the use of NIV for patients in acute respiratory failure. Although NIV offers a less invasive intervention for respiratory distress, the NIV failure rate in patients with pneumonia has been reported as high as 50% [7]. It is very difficult to predict which patients will improve and which will deteriorate [7], and among those who decline there is an increased incidence of peri-intubation complications and a significant increase in mortality [9, 10]. Several possible explanations for this have been proposed, such as the increased metabolic demands in patients with pneumonia, the inability to adequately clear respiratory secretions, and the protracted time course of pneumonia when compared to other common indications for NIV. Possible exceptions to the poor performance of NIV in patients with pulmonary infection

include patients with pneumonia and COPD with hypercapnic respiratory failure. This may be due to overlap in diagnosis between COPD exacerbation and true infection [8]. Other possible exceptions include neutropenic patients with hematologic malignancy, or recent solid organ transplant recipients with suspected pneumonia, possibly because these patients have a higher incidence of viral pneumonia than immunocompetent patients [11–14]. Overall, these data are still relatively sparse. If NIV is attempted in these patients, the clinician should provide near-continuous bedside reassessment and not hesitate to intubate if there is no significant improvement.

Use in Patients with Asthma Exacerbation

NIV has also been used in patients with acute exacerbations of asthma, however there is only limited evidence to help guide the clinician. The available studies fail to demonstrate improvement in mortality or intubation rates, but show an apparent decrease in hospital admission rates, hospital length of stay, symptom severity, and indirect markers of severity, such as pulmonary functions tests or arterial blood gases [15–18]. However, there are no high-quality studies addressing the use of NIV in patients with the most severe forms of asthma exacerbation, limiting any conclusion regarding its impact on mortality and intubation rates in this patient population [19]. For patients with severe asthma exacerbations, NIV should be used with caution, in the context of maximal medical therapy and continuous bedside reassessment.

Use in Patients with ARDS

Limited evidence suggests that NIV might be associated with decreased intubation rates in select patients with early mild ARDS, however overall mortality rates seem to be unchanged, and very close clinical monitoring is required [20–22]. NIV is not appropriate as a first line approach for established ARDS, given the importance of

careful control of tidal volume and airway pressure in this syndrome [23].

Use of NIV in Patients with Altered Mental Status

As mentioned, one of the most common traditional contraindications for the use of NIV is significantly altered mental status, because of the concern that these patients have compromised airway protective reflexes and are not able to adequately manage pulmonary or oropharyngeal secretions. Vomiting into the positive pressure mask is potentially catastrophic in these patients. For intoxicated patients with respiratory distress NIV is almost never the safest alternative, because of unpredictable toxicokinetics and the risk of vomiting. Though NIV can be of great utility in patients with acute exacerbations of COPD, these patients frequently exhibit altered mental status due to hypercapnia. Low to moderate quality evidence suggests that select patients with hypercapnic encephalopathy may warrant a trial of NIV if very close monitoring is feasible [24, 25]. Any such attempt should be aborted if there is no significant improvement in mental status within a short period [24].

Use of NIV for Preoxygenation Prior to Intubation

In carefully selected patients NIV can be used to maximize preoxygenation prior to intubation for acute respiratory failure. By providing high fractional inspired concentrations of oxygen, eliminating alveolar nitrogen, and recruiting atelectatic lung regions, this approach has the potential to improve oxygenation prior to intubation, and extend the “safe apnea time” prior to oxygen desaturation [26]. Patients should generally meet the same entry criteria as for the regular use of NIV, and those who are apneic or whose airway protective reflexes are in doubt are likely not appropriate for this relatively novel use of NIV.

Use of NIV to Facilitate Weaning from Invasive Ventilation

In addition to its use in patients with acute respiratory failure, NIV has also shown some promise for its use in liberating patients from invasive ventilation. Some evidence supports extubation to NIV as a safe strategy in certain patients with resolving acute respiratory failure, such as COPD patients with acute on chronic hypercapnia [27]. This approach may reduce the incidence of some risks associated with prolonged intubation and invasive ventilation, such as ventilator-associated pneumonia and tracheostomy rates. NIV use in this context may also reduce the total duration of ventilation, as well as ICU and hospital length of stay, without a higher risk of reintubation [1, 27–29].

Palliative Care Indications

NIV has been used in an attempt to both enhance short term survival and to optimize comfort in dying patients and those who decline full resuscitative efforts. While mortality among these patients remains high, survivors report no decrease in their quality of life compared to their baseline after the hospitalization, and there are no apparent negative impacts of NIV on their psychological well-being [30, 31]. The topic remains challenging, in particular because it is difficult to predict in which patients there may be a benefit, as opposed to merely an extended dying process with limited ability to communicate, eat, and drink [32]. Decisions about the use of NIV at the end of life are likely best made on an individual patient level, in close collaboration with surrogate decision makers.

Use of High-Flow Nasal Cannula as an Alternative to NIV

The heated high-flow nasal cannula (HFNC) is a relatively new alternative oxygen delivery device that may be of benefit in carefully selected patients with non-hypercapnic acute hypoxic respiratory

failure. In contrast to conventional low-flow nasal cannulae, which provide oxygen flow rates up to approximately 6 L/min, HFNC can deliver flow rates in excess of 40 L/min. The physical characteristics of the device, as well as the addition of a humidifying apparatus and heating circuit, make this a surprisingly comfortable and well-tolerated method of delivering substantial oxygen support [33]. Because it does not involve a tight fitting mask, HFNC is often better tolerated than a conventional NIV interface. This technology is relatively new and the evidence supporting its use is still evolving. Generally speaking, HFNC appears to be a safe and effective alternative for alert patients with certain types of non-hypercapnic respiratory failure. There is probably insufficient ventilatory effect to rely on HFNC in patients with hypercapnia, and the device offers no airway protection. A 2015 multicenter, randomized, open label trial compared HFNC, NIV, and standard oxygen therapy in a relatively large cohort of hypoxemic patients [34]. Approximately 60–70% of these patients had some type of pneumonia. Intubation rates did not differ between the groups, but 90-day mortality was significantly lower in the HFNC group. The reasons for this are unclear. Additionally, NIV confers no mortality or other benefit over oxygen therapy alone, including HFNC patients, in immunocompromised patients with hypoxemic respiratory failure [35]. In the absence of additional evidence, the use of HFNC is probably best individualized to each patient. The overall concern about morbidity associated with delayed intubation in pneumonia patients supported with NIV probably applies equally to HFNC.

References

- Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374(9685):250–9. Epub 2009/07/21.
- Cabrini L, Landoni G, Oriani A, Plumari VP, Nobile L, Greco M, et al. Noninvasive ventilation and survival in acute care settings: a comprehensive systematic review and meta-analysis of randomized controlled trials. *Crit Care Med*. 2015. Epub 2015/01/08.
- Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Hospital patterns of mechanical ventilation for patients with exacerbations of COPD. *Ann Am Thorac Soc*. 2015;12(3):402–9.
- Weitz G, Struck J, Zonak A, Balnus S, Perras B, Dodt C. Prehospital noninvasive pressure support ventilation for acute cardiogenic pulmonary edema. *Eur J Emerg Med*. 2007;14(5):276–9. Epub 2007/09/08.
- Giacomini M, Iapichino G, Cigada M, Minuto A, Facchini R, Noto A, et al. Short-term noninvasive pressure support ventilation prevents ICU admittance in patients with acute cardiogenic pulmonary edema. *Chest*. 2003;123(6):2057–61. Epub 2003/06/11.
- Carrillo A, Gonzalez-Diaz G, Ferrer M, Martinez-Quintana ME, Lopez-Martinez A, Llamas N, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med*. 2012;38(3):458–66. Epub 2012/02/10.
- Carron M, Freo U, Zorzi M, Ori C. Predictors of failure of noninvasive ventilation in patients with severe community-acquired pneumonia. *J Crit Care*. 2010;25(3):540.e9–14. Epub 2010/05/04.
- Confalonieri M, Potena A, Carbone G, Porta RD, Tolley EA, Umberto MG. Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. *Am J Respir Crit Care Med*. 1999;160(5 Pt 1):1585–91. Epub 1999/11/11.
- Wood KA, Lewis L, Von Harz B, Kollef MH. The use of noninvasive positive pressure ventilation in the emergency department: results of a randomized clinical trial. *Chest*. 1998;113(5):1339–46. Epub 1998/05/22.
- Ferrer M, Cosentini R, Nava S. The use of non-invasive ventilation during acute respiratory failure due to pneumonia. *Eur J Intern Med*. 2012;23(5):420–8. Epub 2012/06/26.
- Antonelli M, Conti G, Bui M, Costa MG, Lappa A, Rocco M, et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. *JAMA*. 2000;283(2):235–41. Epub 2000/01/14.
- Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *N Engl J Med*. 2001;344(7):481–7. Epub 2001/02/15.
- Hilbert G, Gruson D, Vargas F, Valentino R, Chene G, Boiron JM, et al. Noninvasive continuous positive airway pressure in neutropenic patients with acute respiratory failure requiring intensive care unit admission. *Crit Care Med*. 2000;28(9):3185–90. Epub 2000/09/29.
- Gristina GR, Antonelli M, Conti G, Ciarlone A, Rogante S, Rossi C, et al. Noninvasive versus invasive ventilation for acute respiratory failure in patients with hematologic malignancies: a 5-year multicenter observational survey. *Crit Care Med*. 2011;39(10):2232–9. Epub 2011/06/15.
- Brandao DC, Lima VM, Filho VG, Silva TS, Campos TF, Dean E, et al. Reversal of bronchial obstruction with bi-level positive airway pressure

- and nebulization in patients with acute asthma. *J Asthma*. 2009;46(4):356–61. Epub 2009/06/02.
16. Gupta D, Nath A, Agarwal R, Behera D. A prospective randomized controlled trial on the efficacy of noninvasive ventilation in severe acute asthma. *Respir Care*. 2010;55(5):536–43. Epub 2010/04/28.
 17. Lim WJ, Mohammed Akram R, Carson KV, Mysore S, Labiszewski NA, Wedzicha JA, et al. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. *Cochrane Database Syst Rev*. 2012;12, CD004360. Epub 2012/12/14.
 18. Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. *Chest*. 2003;123(4):1018–25. Epub 2003/04/10.
 19. Landry A, Foran M, Koyfman A. Does noninvasive positive-pressure ventilation improve outcomes in severe asthma exacerbations? *Ann Emerg Med*. 2013;62(6):594–6. Epub 2013/06/19.
 20. Pichot C, Petitjeans F, Ghignone M, Quintin L. Swift recovery of severe acute hypoxemic respiratory failure under non-invasive ventilation. *Anaesthesiology*. 2014. Epub 2014/10/24.
 21. Zhan Q, Sun B, Liang L, Yan X, Zhang L, Yang J, et al. Early use of noninvasive positive pressure ventilation for acute lung injury: a multicenter randomized controlled trial. *Crit Care Med*. 2012;40(2):455–60. Epub 2011/10/25.
 22. Luo J, Wang MY, Zhu H, Liang BM, Liu D, Peng XY, et al. Can non-invasive positive pressure ventilation prevent endotracheal intubation in acute lung injury/acute respiratory distress syndrome? A meta-analysis. *Respirology*. 2014;19(8):1149–57. Epub 2014/09/12.
 23. Rana S, Jenad H, Gay PC, Buck CF, Hubmayr RD, Gajic O. Failure of non-invasive ventilation in patients with acute lung injury: observational cohort study. *Crit Care*. 2006;10(3):R79. Epub 2006/05/16.
 24. Diaz GG, Alcaraz AC, Talavera JC, Perez PJ, Rodriguez AE, Cordoba FG, et al. Noninvasive positive-pressure ventilation to treat hypercapnic coma secondary to respiratory failure. *Chest*. 2005;127(3):952–60. Epub 2005/03/15.
 25. Scala R. Hypercapnic encephalopathy syndrome: a new frontier for non-invasive ventilation? *Respir Med*. 2011;105(8):1109–17. Epub 2011/03/01.
 26. Weingart SD, Trueger NS, Wong N, Scofi J, Singh N, Rudolph SS. Delayed sequence intubation: a prospective observational study. *Ann Emerg Med*. 2015;65(4):349–55. Epub 2014/12/03.
 27. Burns KE, Meade MO, Premji A, Adhikari NK. Noninvasive positive-pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database Syst Rev*. 2013;12, CD004127. Epub 2013/12/11.
 28. Ornico SR, Lobo SM, Sanches HS, Deberaldini M, Tofoli LT, Vidal AM, et al. Noninvasive ventilation immediately after extubation improves weaning outcome after acute respiratory failure: a randomized controlled trial. *Crit Care*. 2013;17(2):R39. Epub 2013/03/19.
 29. Vaschetto R, Turucz E, Dellapiazza F, Guido S, Colombo D, Cammarota G, et al. Noninvasive ventilation after early extubation in patients recovering from hypoxemic acute respiratory failure: a single-centre feasibility study. *Intensive Care Med*. 2012;38(10):1599–606. Epub 2012/07/25.
 30. Azoulay E, Kouatchet A, Jaber S, Lambert J, Meziani F, Schmidt M, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. *Intensive Care Med*. 2013;39(2):292–301. Epub 2012/11/28.
 31. Nava S, Ferrer M, Esquinas A, Scala R, Groff P, Cosentini R, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. *Lancet Oncol*. 2013;14(3):219–27. Epub 2013/02/15.
 32. Azoulay E, Demoule A, Jaber S, Kouatchet A, Meert AP, Papazian L, et al. Palliative noninvasive ventilation in patients with acute respiratory failure. *Intensive Care Med*. 2011;37(8):1250–7. Epub 2011/06/10.
 33. Ward JJ. High-flow oxygen administration by nasal cannula for adult and perinatal patients. *Respir Care*. 2013;58(1):98–122.
 34. Frat J-P, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185–96.
 35. Lemiale V, Mokart D, Resche-Rigon M, et al. Effect of noninvasive ventilation vs oxygen therapy on mortality among immunocompromised patients with acute respiratory failure: a randomized clinical trial. *JAMA*. 2015;314:1711–9.