Non-Invasive Respiratory Support Strategy in Adults with Acute Respiratory Failure

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Abstract

Patients with acute respiratory failure wil sometimes need invasive mechanical ventilation (IMV). High-demand events such as a pandemic will render the already limited bed in the ICU unavailable for another patient who also needs IMV. Acute respiratory failure can be divided into two categories: hypoxemic respiratory failure and hypercapnic respiratory failure. Non-invasive strategies presently available for treatment of acute respiratory failure are non-invasive ventilation (NIV), continuous positive airway pressure (CPAP), and high flow nasal oxygen (HFNO). Strong evidence has been present for the use of NIV in acute exacerbations of COPD, cardiogenic pulmonary edema, and ARF in immunocompromised patients, while in hypoxemic respiratory failure, there is low to moderate certainty of evidence pointing to the benefit of CPAP and HFNO. Correctly and selectively using these non-invasive strategies can reduce mortality and prevent intubation.

Keywords: ARF, CPAP, HFNO, NIV

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Submitted: December 13th, 2023
Accepted: April 25th, 2024
Published: April 30th, 2024

J Respirol Indones. 2024
Vol. 44 No. 2: 179–86
https://doi.org/10.36497/jri.v44i2.650

INTRODUCTION

The COVID-19 pandemic has exposed a huge gap in our capacity to treat acute respiratory failure (ARF). During the pandemic, even developed countries struggled to provide intensive care and respiratory support due to the high demand. Eventually, this condition also depleted resources for non-COVID respiratory failure patients. Such a situation necessitated tiered respiratory support to be implemented to help as many patients as possible and to ensure patients received the respiratory support level needed, hence the need to understand the use case and efficacy of non-invasive respiratory support strategies.[1]

Respiratory failure is the inability of the respiratory system to perform one or both of its main functions; the first is to provide oxygen for metabolism, and the other is to remove carbon dioxide created from it. From this definition, we usually divide respiratory failure into two types: type 1 (hypoxemic) and type 2 (hypercapnic).[1]

Acute respiratory failure can be life-threatening because sudden derangement of arterial blood gases and acid-base status can disrupt vital metabolism, while chronic respiratory failure usually produces an indolent and slowly progressive clinical picture. Acute respiratory failure is a syndrome rather than a disease; therefore, the respiratory support provided must be tailored based on the disease causing it.[1]

In many cases, both respiratory failures can coexist. The disease that causes hypoxemia can be complicated by processes causing pump failure and hypercapnia. The opposite is also true. Although ARF is defined by the content of arterial oxygen or carbon dioxide concentrations, the major threat to patients is the disruption of oxygen delivery to the tissue, which can disrupt metabolism and many homeostasis processes.[1]

NON-INVASIVE STRATEGY FOR ACUTE RESPIRATORY FAILURE

Securing the airway is the most important component in the management of ARF, hence the popularity of invasive mechanical ventilation (IMV). There are several disadvantages to IMV, namely the need to insert an endotracheal tube (ETT), which is technically challenging and potentially can create another infectious problem such as ventilator-associated pneumonia (VAP) and accompanying complications such as sepsis or septic shock. This disadvantage is profoundly encountered in the group of patients who already develop signs of respiratory failure but who still have intact airway reflexes and do not have excessive secretions so that they are able to protect their own airways. This group of patients will greatly benefit from non-invasive strategies by avoiding intubation.[2]

Non-invasive respiratory support encompasses several different devices, such as non-invasive ventilation (NIV), also known as bi-level positive airway pressure (Bi-PAP), continuous positive airway pressure (CPAP), and high flow nasal oxygen (HFNO). There have been several guidelines describing their use case and level of evidence of their usefulness. For example, NIV's strongest evidence is in acute exacerbations of chronic obstructive respiratory disease (AECOPD) and acute cardiogenic pulmonary edema, while its evidence in acute hypercapnic respiratory failure due to obesity, neuromuscular disease, andchest wall deformity is weaker.[3] Continuous positive airway pressure and HFNO are most likely more useful in hypoxemic respiratory failure cases.[4]

Delivery of the NIV can be performed in different settings, including the emergency room, medical ward, high care unit (HCU), and intensive care unit (ICU), although trained staff and an appropriate monitoring system should be in place. This is due to the fact that the failure of NIV is still about 20–30%; therefore, patient selection and the severity of respiratory failure when NIV was initiated will determine the successful outcome.[5] CPAP can also be delivered from the same machine as NIV/Bi-PAP. On the other hand, HFNO, while also best deployed in place with monitoring systems, has advantages in simpler setup, maintenance, training, and monitoring. It also tends to be better tolerated by patients due to its nasal prong interface and the warm and humidified flow of oxygen it produces.[5,6]

PHYSIOLOGY OF NON-INVASIVE RESPIRATORY SUPPORT STRATEGIES

Respiratory disorders could create distortions in lung compliance, the amount of pressure required to expand the lung. This pressure is known as transpulmonary pressure (TPP), which is expressed as alveolar pressure minus pleural pressure. Both increases and decreases in lung compliance can create difficulty breathing. Increased compliance, such as emphysema, will make it harder for TPP to expand more volume into the lung because it is already in high volume during rest. Decreased compliance, such as acute cardiogenic pulmonary edema or acute respiratory distress syndrome, will also make it harder to expand the lungs due to the resistive effect of air-filled alveoli.[7]

The provision of respiratory support through the patient's upper airway by a mask or similar device without using invasive means such as an endotracheal tube is the definition of non-invasive ventilation. Usually, bi-level positive airway pressure (BPAP) is applied to keep the airway secure.[5] Different pressure supports will be delivered during inspiration and expiration, namely inspiratory positive airway pressure (IPAP) and expiratory airway pressure (EPAP). This pressure difference will drive and augment ventilation for the patient.[8] Non-invasive ventilation reduces the work of breathing through several mechanisms. The generation of EPAP will prevent airway collapse, thus reducing the initial work of initiating inspiration, while IPAP will augment TPP, therefore reducing the main work of breathing load.[7]

On the other hand, CPAP provides continuous pressure support in the form of positive end expiratory pressure (PEEP), which basically has the same effect as EPAP, but it does not support or augment patient tidal volume or minute ventilation.

CPAP provides constant pressure support during inspiration and expiration; therefore, it creates a pneumatic splint of the upper airway, preventing it from collapsing during sleep and preventing small airways from collapsing during end expiration, hence improving oxygenation.[1]

High-flow nasal oxygen can deliver high-concentration oxygen with constant FiO_2 and higher flow than conventional oxygen therapy, up to 60 L/minute. The high flow can help wash out CO_2, and the high concentration of oxygen will create an oxygen reservoir in the upper airway, which will reduce dead space. A higher flow of oxygen can also create positive pressure in the upper airways, and this can be transmitted to the small airways as PEEP, thereby giving a similar positive effect as CPAP on the respiratory process, although in smaller ways.[9]

ACUTE HYPERCAPNIC RESPIRATORY FAILURE

Acute hypercapnic respiratory failure (AHCRF) is defined by $PaCO_2$ >45 mmHg with accompanying acidemia, usually caused by defects in one or more respiratory pump components (CNS, peripheral nerves, respiratory muscles, and airway) causing insufficient ventilation to maintain normal $PaCO_2$. Rapid elevation of $PaCO_2$, as happens in acute events, will result in a drop in arterial pH causing many metabolic disturbances. Most AHCRF is caused by acute exacerbations of COPD, for which NIV is the standard treatment. However, there are other conditions in which respiratory pump failure also causes AHCRF, so NIV is also used in wide-ranging AHCRF etiologies such as cystic fibrosis, chest wall deformity, neuromuscular disease, and obesity/obesity hypoventilation syndrome. The use of NIV in these other etiologies is not as extensively researched as the use of NIV in AECOPD.[3,5]

The use of NIV in AECOPD patients with ARF is consistently shown to reduce mortality, prevent intubation, and reduce the risk of nosocomial pneumonia. The current ATS/ERS guidelines recommend using NIV in AECOPD patients with pH ≤7.35, $PaCO_2$ >45, and a respiratory rate >20–24 breaths per minute despite adequate medical therapy. Within the range of pH indicated for NIV initiation, less severely ill patients with a pH of 7.25–7.35 can benefit from NIV by resolving acidosis, preventing endotracheal intubation, and preventing invasive mechanical ventilation (IMV). The more severely ill patient with a pH <7.25 can benefit from NIV, not to prevent intubation but as an alternative to intubation and IMV. There is no absolute lower limit of pH for which NIV is contraindicated. However, more severe acidosis requires close monitoring and immediate access to intubation and IMV. However, the use of NIV in patients with hypercapnia but without acidosis is not recommended because there is no significant improvement compared to conventional oxygen and standard medical treatment.[8,10,11]

Initiation of NIV compared to IMV in AECOPD has yielded a better outcome for patients by reducing mortality and hospital length of stay. However, the need for NIV in AECOPD itself is a poor prognostic factor for 1-year mortality risk. Garcia-Sanz et al reported a 1-year mortality risk of 26.2% and a 5-year mortality risk of 64.3%. This was because patient who need NIV usually older, have more severe COPD and complicated comorbidity.[11,12] Successful NIV as an alternative to IMV has the added benefit of reducing ICU and hospital admissions, incidents of ventilator-associated pneumonia, and tracheostomy.

Despite the formal criteria for initiation of NIV and the increasing familiarity of NIV outside ICU, the failure rate of NIV is still significant and reported to be about 20–30%. This emphasizes the need for correct patient selection, timing, interface used, environment where NIV is being used, and a standardized predictor for NIV failure (Figure 1). Failure of NIV is associated with a higher mortality and a longer stay in the ICU. Several predictors for NIV failure are a higher APACHE II score (>20.5) at presentation and persistent hypercapnia and/or acidosis.[13] Whenever possible, the possibility of failure needs to be considered when withdrawing NIV and replacing it with IMV or allowing a more conservative approach (not using NIV) if palliation is the preferred outcome.[11]

Correct Patient

- Strong evidence for NIV/BPAP
  - COPD exacerbation with hypercapnia
  - Cardiogenic pulmonary edema
  - Immunocompromised patient with ARF
- Low-moderate certainty of evidence for CPAP and HFNO
  - Acute hypoxemic respiratory failure due to pneumonia, ARDS, COVID-19
  - Alternative to NIV in hypercapnic respiratory failure

Correct timing

- Patient with Intact airway reflexes
- NIV/BPAP : pH ≤7.35, $PaCO_2$ > 45, RR > 20-24 despite standard therapy
- CPAP/HFNO : Hypoxemia despite optimal conventional oxygen therapy

Correct termination

- Perform intubation if there is no improvement in clinical condition, pH, PCO_2 or PO_2 after 1-2 hours of application

Correct equipment and staff

- correct interface should be used and fit well enough
- helmet interface should be considered in NIV/CPAP
- The ward should have staff with proper training and proper monitoring equipment

Figure 1. Consideration for application of non-invasive strategies[3–5,10,16,17]

High-flow nasal oxygen can be considered an alternative to NIV by virtue of its capability to provide constant FiO_2, generation of positive airway pressure up to 7 cmH_2O, and humidified and warmed inspired air, which can improve mucociliary clearance.[9,14] Xu, et al. conducted a meta-analysis of 10 studies involving 1265 patients with hypercapnic respiratory failure. The use of HFNO compared to NIV resulted in comparable mortality, the need for IMV and ABG improvement with the added benefit of comfortability, and reduced side effects. However, HFNO patients with a pH <7.30 would most likely need crossover or rescue therapy with NIV, and these patients would need a longer interval with NIV, although the rate of intubation was similar. Additionally, this study also showed that HFNO could reduce the need for NIV in stable hypercapnic patients without acidosis compared with conventional oxygen therapy.[14]

Although HFNO is not a first-line treatment for AHCRF, its use can be considered in AECOPD patients not severe enough to warrant NIV, i.e., patients with hypercapnia but not acidosis, and for patients whose NIV is contraindicated. The main advantage of HFNO over NIV is patient tolerance because HFNO, with its nasal prongs, is more comfortable and allows for communication and feeding to be conducted. This is important because intolerance to NIV interface is one of the causes of NIV failure. HFNO might also beconsidered for the purpose of filling in the gap between NIV for feeding, medication, for patients with discomfort from NIV but still willing to continue NIV, or for patients who outright decline NIV.[11,14,15]

Other cause of hypercapnic respiratory failure due to tuberculosis infection prevalent in Indonesia is non-cystic fibrosis (CF) bronchiectasis. It is characterized by permanent distortion of the airways with inflammation and mucus plugging, with clinical manifestations of chronic cough with productive sputum, breathlessness, and an obstructive pattern on spirometry. Acute exacerbations resulting in respiratory failure are not uncommon in these patients and might give a similar presentation as patients with AECOPD. Establishment of intubation and IMV in this group of patients will have high mortality and morbidity. However, the use of NIV in non-CF bronchiectasis has not been thoroughly studied, and the data is still lacking.

Phua, et al. conducted a retrospective study of patients with bronchiectasis and found that NIV failure happened in 1/3 of patients, while Hadda et al conducted a retrospective study of patients with non-

CF bronchiectasis who experienced acute respiratory failure. More than half (52.45%) had tuberculosis as the etiology of bronchiectasis, and all had hypercapnia and acidosis on arterial blood gas (ABG). Of note, the presence of COPD is not confirmed due to a lack of spirometry data. Almost 2/3 of patients were successfully treated with NIV, with notable findings of correction of pH and PCO_2 parameters that were comparable with those on IMV. The failure rate of these 2 retrospective studies is higher than NIV failure in AECOPD (20%), but still showed the feasibility of NIV as a first-line treatment in non-CF bronchiectasis patients with ARF. When given as first-line treatment, NIV reduces mortality and length of stay at the hospital. In cases of NIV failure, there is no notable increase in mortality or length of stay at the hospital.[18,19]

ACUTE HYPOXEMIC RESPIRATORY FAILURE

Acute hypoxemic respiratory failure (AHORF) is defined by an arterial PaO_2 <60 mmHg and is usually caused by several factors, i.e., low inspired oxygen fraction, hypoventilation, ventilation/perfusion (V/Q) mismatch, shunt, or diffusion problem. De novo ARF is defined as respiratory failure without underlying chronic disease or pulmonary edema; most AHORF patients are part of this group, mainly represented by pneumonia and/or acute respiratory distress syndrome (ARDS). The use of NIV in this patient group is still controversial. This is due to the substantial difference in pathogenesis and physiological alteration, which happened mainly not in the respiratory pump but in the alveoli and pulmonary vasculature and involved complex inflammatory process. Therefore, NIV only has a limited and specific use case, i.e., in cardiogenic pulmonary edema and immunocompromised patients.[1,2,10]

Cardiogenic pulmonary edema causes hypoxemia by reducing lung compliance and increasing work of breathing due to congestion. Hypercapnia sometimes can occur, creating mixed respiratory failure. In patients not responding to standard medical treatment, the application of positive pressure via mouth, either using CPAP or an NIV, can reduce the work of breathing and improve hypoxemia by reducing left ventricular preload and afterload. This beneficial effect is produced whether hypercapnia is present or not. Multiple trials have shown that NIV and CPAP can reduce the need for intubation and hospital mortality. It also clarifies that NIV/CPAP use in cardiogenic edema is not associated with myocardial infarction.[1,3,5,10]

Immunocompromised patients, especially those due to transplant and malignancy, are often experiencing the threat of ARF, which requires ICU treatment. The use of NIV and CPAP in this group with mild to moderate ARF can improve survival. Paula, et al. showed that in immunocompromised patients due to malignancy and transplant, NIV could reduce the need for intubation and improve survival. This effect is important for this group because IMV and further ICU treatment can have profound complications, such as ventilator-associated pneumonia. Although other studies did not find a reduction in intubation and mortality using NIV, ERS/ATS still recommended using early NIV/CPAP in immunocompromised patients with ARF because the benefits outweigh their undesirable effects.[10,20]

Lack of efficacy from NIV to reduce the work of breathing in ARDS is in contrast with NIV efficacy in AECOPD. The use of NIV can reduce the work of breathing only after significant pressure support has been added. This large pressure will result in a larger tidal volume, which can exacerbate lung injury, especially if prolonged; thus, the use of lung protective ventilation will be much more difficult with NIV. Gastric insufflation, air leaks, and patient intolerance will also complicate the application of NIV. Therefore, IMV is the therapy of choice because it can be used to deliver low tidal volume ventilation consistently, reduce the work of breathing, and be used with total patient paralysis if needed.[10]

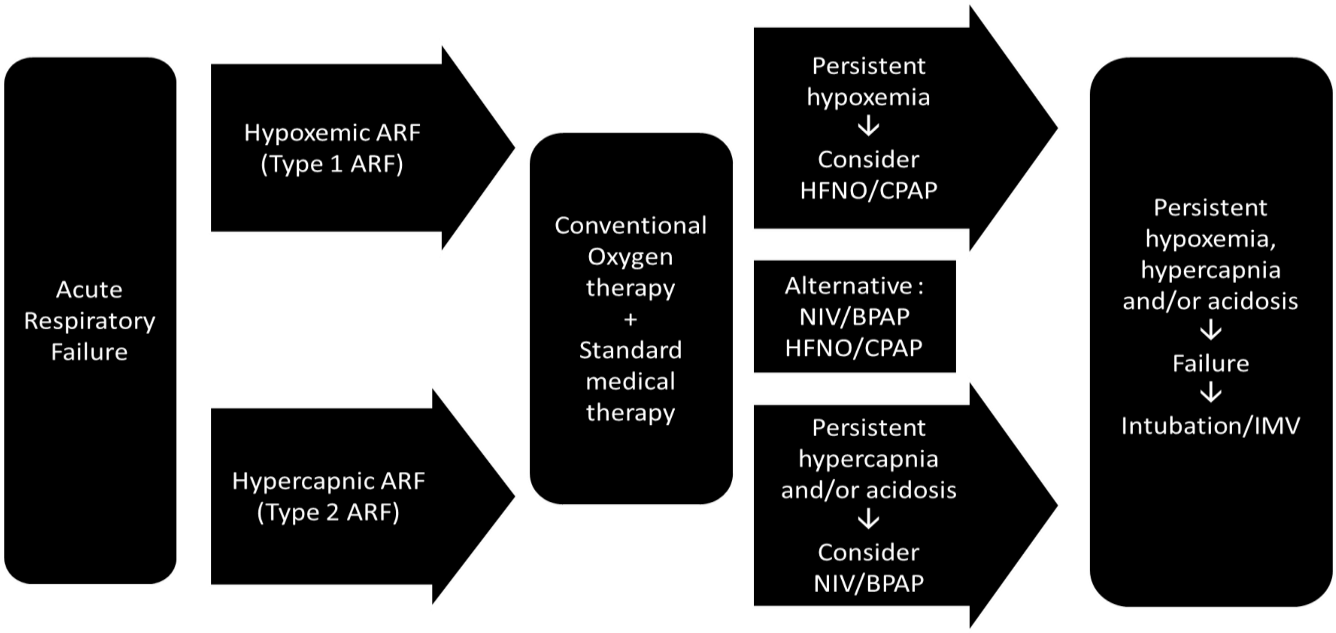

Figure 2. Management of acute respiratory failure treatment using NIV

Failure of NIV in de novo ARF can be predicted early by a higher severity score (APACHE II or SOFA), older age, pneumonia and/or ARDS as etiology, and lack of improvement after 1 hour. Another disadvantage of using NIV in this group is the risk of delaying intubation and a poorer outcome due to NIV patients having a larger tidal volume and developing more complications after switching to NIV. It was also shown that failure of NIV will worsen the prognosis for de novo ARF; therefore, ERS/ATS did not make any recommendation for the use of NIV in de novo ARF. If the choice of using NIV is made with aim to prevent intubation, then careful patient selection and sufficient precaution as not to delay intubation must be made.[10]

Although IMV is the go-to strategy for ARF not responding to conventional oxygen therapy, sometimes circumstances and conditions do not allow for it, for example, during a pandemic. Non-invasive strategies have the potential to become a bridge between conventional oxygen therapy and IMV in the hope that some patients can avoid intubation. Sakuraya, et al. found that in AHORF patients with etiology mainly of pneumonia, CPAP reduces short-term mortality and has a lower intubation rate compared to COT. Ferreyro, et al. also obtained that non-invasive strategies using helmet NIV and face mask NIV could reduce mortality and intubation rate, while using HFNO was associated with a decrease in intubation rate but not with mortality. Pitre, et al. also found that helmet CPAP might reduce mortality, while HFNO might reduce the need for intubation.[4,16,17]

During the COVID-19 pandemic, discussion around the choices of non-invasive respiratory support strategies re-emerged because the abundance of AHORF cases due to COVID-19 pneumonia and ARDS. There is a conflicting report on the merits of HFNO and NIV in preventing intubation and in reducing mortality, where some studies report a decrease in intubation rate and mortality, while others only report a reduction in intubation rate or mortality but not both, or even report no significance at all. This difference can be explained by the difference in sample population characteristics, severity of disease, and methodology used, but this difference signalled that at least a non-invasive oxygenation strategy is better than COT and can somewhat reduce the burden of IMV and mortality if used in a selected population.[21]

Data from Indonesia is quite limited, mostly case report series. Baskoro, et al. found that adult patients with respiratory failure treated in the ICU responded favorably in the first 3 hours of observation with the initiation of NIV, with significant clinical improvement in respiratory rate, PaO_2/FiO_2 ratio, and

PCO_2 level. Agustin, et al. stated that the use of NIV and HFNO in emergency and ICU patients with COVID-19 hypoxia could improve respiratory rate and oxygen saturation. Soebekti, et al. also reported similar findings but showed that in COVID-19-related respiratory failure, after 24 hours of using HFNO, only less than half of the patients would show clinical improvement, prevent intubation and avoid mortality. The rest will eventually need intubation or succumb to the disease.[22–24]

Results from these meta-analysis and most other studies are encouraging but need to be viewed with caution due to the low certainty of the evidence. Therefore, the use of a non-invasive strategy needs to be used selectively and monitored carefully, and IMV should be ready to deploy in case of worsening condition occurs (Figure 2).

CONCLUSION

Noninvasive oxygenation strategies such as NIV, CPAP, and HFNO can be used effectively in selected groups of patients with acute hypercapnic and/or acute hypoxemic respiratory failure. It can reduce the need for intubation and IMV, lower mortality and hospital length of stay if used correctly. This represents huge untapped potential in the management of acute respiratory failure, especially in Indonesia, where its use is still limited, mostly in intensive care settings.

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