28 Noninvasive Mechanical Ventilation in Hypoxemic Respiratory Failure: Determinants of Response and Patients' Flow Chart Recommendations – Key Topics and Clinical Implications

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Abbreviations

ACPE	Acute cardiogenic pulmonary edema
DNI	Do not intubate
ETI	Endotracheal intubation
IBW	Ideal body weight

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NPPV Non-invasive positive pressure ventilation
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PEEP Positive end-expiratory pressure
PS Pressure support
Vt Tidal volume

28.1 Introduction

Acute hypoxemic respiratory failure (AHRF) is one of the most common conditions of severe dyspnea seen in the emergency department. This chapter summarizes the main indications for noninvasive positive pressure ventilation (NPPV) in AHRF, with a focus on evidence, clinical recommendations, and practical points.

28.2 Acute Cardiogenic Pulmonary Edema

The literature and rationale for noninvasive ventilation (NIV) use in acute cardiogenic pulmonary edema (ACPE) are discussed in detail in Chap. 27 of this book; we summarize it briefly here:

- NIV treatment in ACPE significantly reduces endotracheal intubation (ETI) and mortality, as evidenced by several systematic reviews and a meta-analysis.
- The number needed to treat (NNT) for ETI is 8 and is 13 for mortality. Therefore, there is a strong recommendation for NIV in ACPE, based on a high level of evidence.
- ACPE is also effectively treated with NIV in the prehospital setting.

When treating a patient with ACPE in the emergency department, two main clinical questions must be answered:

1. Should the patient with hypercapnia be treated with bi-level NPPV rather than CPAP?
2. Does the patient with hypertensive ACPE have a different prognosis compared with a patient who is nonhypertensive?

28.2.1 Bi-level NPPV Versus CPAP: Are Two Better than One?

As many as 50 % of patients treated with NIV for ACPE present with acute respiratory failure. This is due to muscle fatigue induced by a remarkable decrease of compliance resulting from sudden alveolar flooding. The theoretical advantage for muscle workload of the addition of pressure support (PS) to positive end-expiratory pressure (PEEP) versus continuous positive airway pressure (CPAP) is not demonstrated in the literature. Several randomized studies and a meta-analysis showed

faster relief of respiratory acidosis; however, neither ETI nor mortality differed significantly between the two modalities. The Cochrane Review on NPPV efficacy in ACPE concludes, "CPAP may be considered the first option in selection of NPPV due to more robust evidence for its effectiveness and safety and lower cost compared with bilevel NPPV" [1]. This may be explained by the rapid favorable effects of PEEP application on both respiration (alveolar recruitment + compliance increase) and circulation (venous return decrease + left ventricle transmural pressure decrease). In summary, in patients with ACPE who have acute respiratory acidosis, NIV and CPAP are equivalent; hence, our advice is to use the treatment that you prefer and are most familiar with.

28.2.2 Hypertensive Versus Nonhypertensive ACPE: Blood Pressure Matters

As many as 50 % of patients treated with NIV for ACPE present with hypertensive crisis, that is, arterial blood pressure ≥140/90 mmHg. Cardiogenic shock associated with ACPE has a much greater mortality. The question is whether nonhypertensive ACPE patients have a worse prognosis than those with hypertensive ACPE. Several studies observed that mortality significantly increases in patients presenting to the emergency department with blood pressure <140/90 mmHg when treated either with NIV or standard therapy. This means that, especially in these patients, the search for a possibly reversible cause of ACPE is mandatory [2]. The comprehensive approach to patients with ACPE should include the assessment of lung involvement, volemia, and heart dysfunction to identify reversible causes such arrhythmias, myocardial ischemia, or valvular dysfunction with bedside ultrasound.

Summary

1. NIV is effective in the treatment of ACPE (Evidence A; NNT = 8 for ETI, NNT = 13 for mortality).
2. NIV can be started effectively in the prehospital setting.
3. Patients with acute respiratory acidosis can be treated with either CPAP or NPPV, provided that the patient does not have any preexisting respiratory muscle overload.
4. Reversible causes (e.g., ischemia, arrhythmias, valvular disease) should be identified.
5. Patients without hypertensive response have a worse prognosis.

28.2.3 NIV for ACPE in Practice

- An initial PEEP level of 10 cmH_2O is probably the best choice.
- If CPAP is used, high-flow stand-alone devices are preferred.
- If bi-level NPPV is used, apply a PS of 10–15 cmH_2O on top of PEEP 8–10 cmH_2O, closely monitoring patient-ventilator interaction, respiratory rate (RR), and tidal volume (Vt).

- Titrate FiO_2 to a SpO_2 >94 %.
- Titrate PS level to obtain a Vt ≤6 ml/kg ideal body weight (IBW) and a RR <25 bpm.
- Increase PEEP up to 12–15 cmH_2O if necessary.
- Set the minimal inspiratory trigger to avoid auto-triggering.
- Set a short rise time according to RR.
- Set a late expiratory trigger (e.g., 20–40 %).
- After 30 min of NIV, reassess arterial blood gases to evaluate both oxygenation and ventilation.

During NIV, serial monitoring of clinical and laboratory values is mandatory:

- Search for any reversible cause (e.g., ischemia, arrhythmias, valvular disease).
- Chose a mask or helmet according to patient preference.
  - Assess patient comfort and leaks.
  - Assess patient-ventilator interaction and synchrony (ineffective efforts, double triggering, auto-triggering).
  - Measure RR and adjust ventilator settings, aiming for a RR ≤25 bpm.
  - Monitor Vt, aiming for ≤6 ml/kg IBW.
  - Repeat arterial blood gas tests for oxygenation and CO_2 monitoring.

28.3 Acute Respiratory Distress Syndrome

Evidence for the use of NPPV in acute respiratory distress syndrome (ARDS) is scant and heterogeneous, however sound knowledge of the pathophysiology of ARDS and ventilator-induced lung injury (VILI) may guide clinicians in deciding whether to apply NIV. The literature and the rationale for NIV use in ARDS are discussed in detail in Chap. 50 of this book, but we summarize it briefly below:

1. In the case of NIV in AHRF, patients with ARDS have worse outcomes [7, 8].
2. NIV in ARDS is accompanied by a high failure rate (up to 70 % [6]), and NIV failure is associated with increased mortality [10].
3. Patients with successful NIV have a low mortality rate (around 20 %) [10], but this may be due to selection of less severe patients.

The main clinical goals for the use of NIV in ARDS should be the following:

- Reversal of hypoxemia
- Prevention of muscle fatigue and severe hypercapnia
- Attenuation of dyspnea and respiratory distress
- Prevention of VILI

Table 28.1 Berlin definition of ARDS from Ferguson et al. [10]

	Acute respiratory distress syndrome		
Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules		
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload; need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
	Mild	Moderate	Severe
Oxygenation[b]	200< PaO_2/FiO_2 ≤300 with PEEP or CPAP ≥5 cmH_2O[c]	100< PaO_2/FiO_2 ≤200 with PEEP ≥5 cmH_2O	PaO_2/FiO_2 ≤100 with PEEP ≥5 cmH_2O

ARDS acute respiratory distress syndrome, *PaO_2* partial pressure of arterial oxygen, *FiO_2* fraction of inspired oxygen, *PEEP* positive end-expiratory pressure, *CPAP* continuous positive airway pressure, *N/A* not applicable

[a]Chest X-ray or CT scan

[b]If altitude is higher than 1000 m, a correction factor should be applied as follows: $PaO_2/FiO_2 \times$ (barometric pressure/760)

[c]This may be delivered noninvasively in the mild ARDS group

According to the Berlin definition of ARDS [9], patients can be stratified into three different categories based on their initial PaO_2/FiO_2 ratio while on at least 5 cmH_2O of PEEP (see Table 28.1). Given the above considerations, we recommend considering NIV only in patients not requiring immediate intubation (approximately 15 % of ARDS patients) [10] and those without significant hemodynamic impairment or severe metabolic acidosis [6].

In patients considered for a NPPV trial:

- Ensure the appropriate environment for NPPV delivery (intensive care unit or high dependency unit) and appropriate ventilator availability (no home ventilators).
- Use an oronasal mask as interface to minimize leaks.
- NIV is preferred over CPAP use, especially in patients with marked distress and hypercapnia. ARDS is generally accompanied by an increased respiratory drive and places great stress on the respiratory muscles. Attenuation of inspiratory effort with PS is advisable. Another important advantage of NIV over CPAP is the ability to closely monitor Vt, which must be maintained below 6 ml/kg IBW.
- Start with a low PEEP level: 5 cmH_2O is probably the best choice, as it allows for subsequent reassessment of the degree of hypoxemia and appears to improve patient stratification [11].
- Apply a PS of 10–15 cmH_2O, closely monitoring patient-ventilator interaction, RR, and Vt.
- Titrate FiO_2 to a SpO_2 >94 %.

- After 30 min of NIV, reassess arterial blood gases.
  - If PaO_2/FiO_2 ratio is <200, the patient has moderate to severe ARDS. Invasive mechanical ventilation is indicated [11].
  - If PaO_2/FiO_2 ratio is >200, the patient has mild ARDS and may be treated with NIV in this phase.
  - If hypercapnia with respiratory acidosis has developed or worsened (i.e., pH <7.3 with $PaCO_2$ >50 mmHg), consider invasive mechanical ventilation.

Once it has been established that a patient has mild ARDS on NIV with 5 cmH_2O of PEEP and does not have significant or worsening respiratory acidosis:

1. Titrate PS level to obtain a Vt ≤6 ml/kg IBW and a RR <25.
2. Titrate FiO_2 to maintain a SpO_2 ≥94 %.
3. Increase PEEP up to 10 cmH_2O if necessary.

During NIV, serial monitoring of clinical and laboratory values is mandatory:

- Assess patient comfort and leaks.
- Assess patient-ventilator interaction and synchrony (ineffective efforts, double triggering, auto-triggering).
- Measure respiratory rate and adjust ventilator settings, aiming for a RR ≤25 bpm.
- Monitor Vt, aiming for ≤6 ml/kg IBW.
- Repeat arterial blood gases for oxygenation and CO_2 monitoring.

Maintain a low threshold for ETI and invasive mechanical ventilation in ARDS patients. Delaying a necessary intubation may harm patients and increase mortality [10].

28.4 Pneumonia

The scant literature on randomized and observational studies in the immunocompetent population does not allow for a strong recommendation for NIV for the treatment of acute respiratory failure in the course of pneumonia. The explanation for the difference of success in comparison with ACPE is twofold: (1) the effects of medical treatment on pneumonia takes much longer; and (2) the favorable effect of PEEP on oxygenation depends on the pattern of lung involvement (greater recruitment in interstitial than in consolidation), and its cardiovascular effects may be remarkably deleterious.

The results of randomized and observational trials in the immunocompromised population are more encouraging, because ETI – the alternative to NIV for severe acute respiratory failure – is frequently complicated by severe infections and a high mortality. Hence, NIV use in the immunocompromised population may decrease intubation rate and improve outcome.

According to the literature, the following suggestions can be made on the probability of NIV success in pneumonia in the immunocompetent population. The outcome is significantly better in patients with preexisting chronic cardiocirculatory or

obstructive lung disease than in those with de novo acute respiratory failure [3]. Finally, early treatment of severe hypoxemic pneumonia with helmet CPAP may effectively reduce the risk of meeting ETI criteria compared with oxygen therapy [4].

Summary

1. NIV is effective in the immunocompromised population.
2. NIV is more effective in acute-on-chronic versus de novo respiratory failure.
3. In immunocompetent patients without a do not intubate (DNI) order, a cautious early NIV trial may be attempted (the interface is a key factor).
4. In immunocompetent patients with a DNI order, NIV is a possible ceiling treatment (the interface is a key factor).

28.4.1 NPPV for Pneumonia in Practice

- An initial PEEP level of 5–8 cmH_2O is probably the best choice.
- If your choice is CPAP, high-flow stand-alone devices are preferred.
- The interface is crucial; helmet CPAP may be better tolerated because treatment is generally longer than two days.
- If your choice is bi-level NPPV, apply a PS of 10–15 cmH_2O on top of PEEP 5–8 cmH_2O, closely monitoring patient-ventilator interaction, RR, and Vt.
- Titrate FiO_2 and PEEP to a SpO_2 >94 %.
- Test the best PEEP, according to PaO_2/FiO_2 ratio, pCO_2, and vital signs responses.
- Titrate PS level to obtain a Vt ≤6 ml/kg IBW and a RR <25 bpm.
- Increase PEEP up to 10–12 cmH_2O if necessary, according to PEEP test.
- Set the minimal inspiratory trigger to avoid auto-triggering.
- Set a short rise time according to respiratory rate.
- Set a late expiratory trigger (e.g., 20–40 %).
- After 30 min of NIV, reassess arterial blood gases to evaluate both oxygenation and ventilation.

During NIV, serial monitoring of clinical and laboratory values is mandatory:

- Treat and monitor clinical response to sepsis (antibiotics, fluids, lactate clearance, etc.).
- Chose the interface according to patient preference; a long NIV course is expected, therefore, a helmet might be preferable.
  - Assess patient comfort and leaks.
  - Assess patient-ventilator interaction and synchrony (ineffective efforts, double triggering, auto-triggering).
  - Measure RR and adjust ventilator settings, aiming for a RR ≤25 bpm.
  - Monitor Vt, aiming for ≤6 ml/kg IBW.
  - Repeat arterial blood gases for oxygenation and CO_2 monitoring

Maintain a low threshold for ETI and invasive mechanical ventilation.

28.5 Blunt Chest Trauma and Atelectasis

NIV in atelectasis is reviewed in detail elsewhere in this book. Trauma patients frequently develop acute respiratory failure resulting from ventilation perfusion mismatching and shunt because of lung contusion, atelectasis, inability to clear secretions, or pneumothorax and/or hemothorax. The rationale for NIV is alveolar recruitment and chest stabilization to prevent ETI and its complications that may lead to adverse outcomes. Randomized trial excluded patients with either severe hypoxemia (PaO_2/FiO_2 <200), respiratory acidosis, or multiorgan dysfunction because they are usually unable to cooperate or protect the airway or clear secretions [5]. Time is a key factor, inasmuch as early treatment is associated with better outcome; further, a lack of response at 1–4 h should promptly lead to intubation and invasive mechanical ventilation. Patient selection seems to be the most important prognostic factor for improved outcome of NPPV treatment of acute respiratory failure due to blunt chest trauma.

Summary

- NIV may decrease both ETI and mortality provided that:
  Patients are treated during early acute respiratory failure
- NIV is used only in hypoxemic non-hypercapnic patients
- NIV is used only in patients without other organ failures
- Other medical and surgical treatments are added to NIV

28.6 Acute Respiratory Failure After Drowning

Acute respiratory failure after drowning is a common event, but its severity spans from rapidly reversible mild hypoxemia to full-blown ARDS. For an in-depth review of the pathophysiology of drowning and the applications of NIV, see Chap. 50 in this book.

Drowning involves aspiration of water into the airways, which directly damages alveolar surface, washes surfactant, and increases lung weight determining atelectasis. Additionally, reflex bronchospasm contributes to hypoxia and respiratory distress while increased permeability in the lung induces pulmonary edema (Szpilman D Drowning *NEJM* 2012). Interestingly, drowning appears to be associated with rapidly reversible respiratory failure [14], thus often requiring short-term ventilatory support. After rescue from water, patients may present with cardiac arrest, generally associated with pulseless electrical activity. Cardiac arrest in this situation is generally hypoxic in nature (especially in the young population) and thus mandates rapid administration of oxygen and ventilatory assistance as well as reversal of hypothermia.

In hemodynamically stable patients, respiratory symptoms may vary from cough and rales (presentation associated with low mortality rates) to severe hypoxemia, cough, and foamy secretions (mortality around 20 % [13]).

Administration of oxygen and SpO_2 monitoring for at least 8 h are advisable in all patients, but those presenting SpO_2 <94 % and signs of respiratory distress may deserve treatment with NIV before considering ETI [15]. NIV may be applied in the prehospital period if indications for emergency ETI are not met.

The main concerns with NIV use in drowned patients are the inability to fully protect the airway and sudden vomiting and aspiration. Given the pathophysiology of drowning, it seems logical to start with noninvasive CPAP, which is usually more widely available and easier to manage. Helmet or full face mask may be used according to availability and staff experience. We recommend starting CPAP with a continuous high-flow delivery system (Venturi system) to avoid CO_2 rebreathing and maximize oxygen delivery to the patient, starting with a PEEP of 10 cmH_2O and titrating FiO_2 to achieve a SpO_2 >94 %. Alternatively, NIV can be started with a PEEP of 10 cmH_2O and a PS level titrated to the patient's need, aiming for a Vt of 6–8 ml/kg IBW (usually around 10 cmH_2O). NIV may be better than CPAP in patients presenting with hypoxic-hypercapnic respiratory failure, provided no alterations in neurologic status exist. Foamy secretions certainly represent a challenge, but clinicians must remember that they are the result of increased permeability in the lung and may thus be controlled or reduced with positive airway pressure.

After NIV or CPAP initiation, neurologic status, RR, blood pressure, and SpO_2 should be closely monitored during the first 1–2 h. Arterial blood gas tests should then be performed. If oxygenation is improving after 60–120 min of CPAP or NIV and no hypercapnia has developed, patients may continue treatment. However, if oxygenation fails to improve or signs of respiratory muscle fatigue are present (including respiratory acidosis), ETI must be performed and invasive mechanical ventilation started. Prognostic factors associated with favorable outcome after drowning are short submersion time and symptom severity after rescue, with worse prognosis in case of cardiac arrest (up to 90 % mortality).

Key Major Recommendations (Fig. 28.1)

- Patients with ACPE should be treated with either CPAP or NIV (strong recommendation).
- In patients with ARDS, NIV is preferred over CPAP. If a cautious trial fails within 1 h, prompt intubation is required.
- In immunocompromised patients with pneumonia, early treatment with NIV may avoid the need for intubation.
- In immunocompetent patients with pneumonia, early treatment is recommended with NIV. The interface is crucial (a helmet is better tolerated). Test a short trial. Pay attention to sepsis.
- In patients with blunt chest trauma: start early, only in hypoxaemic patients and those without other organ failures.

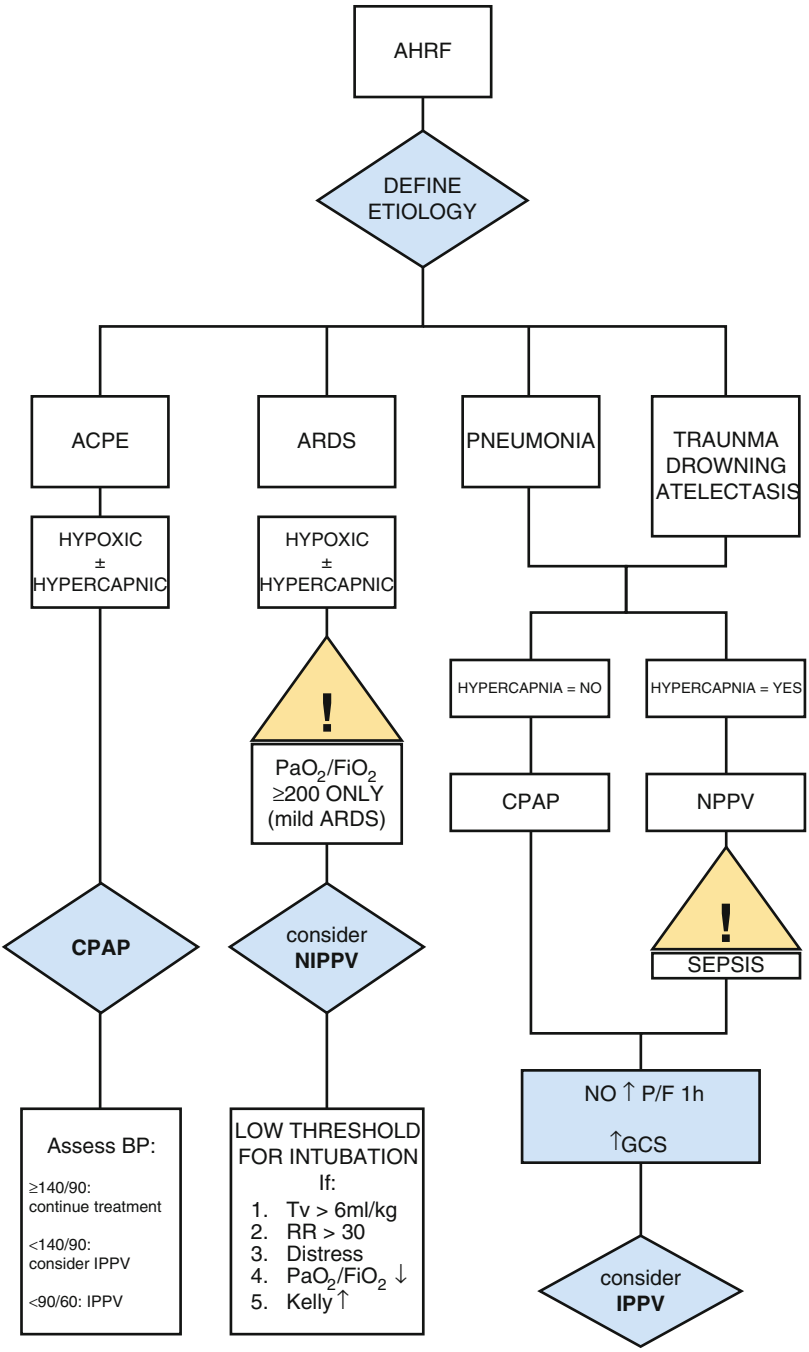

Fig. 28.1 Algorithm for initial management of acute hypoxaemic respiratory failure with NIPPV

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