

## Heart failure/cardiomyopathy

# Indications and practical approach to non-invasive ventilation in acute heart failure

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In acute heart failure (AHF) syndromes significant respiratory failure (RF) is essentially seen in patients with acute cardiogenic pulmonary oedema (ACPE) or cardiogenic shock (CS). Non-invasive ventilation (NIV), the application of positive intrathoracic pressure through an interface, has shown to be useful in the treatment of moderate to severe RF in several scenarios. There are two main modalities of NIV: continuous positive airway pressure (CPAP) and pressure support ventilation (NIPSV) with positive end expiratory pressure. Appropriate equipment and experience is needed for NIPSV, whereas CPAP may be administered without a ventilator, not requiring special training. Both modalities have shown to be effective in ACPE, by a reduction of respiratory distress and the endotracheal intubation rate compared to conventional oxygen therapy, but the impact on mortality is less conclusive. Non-invasive ventilation is also indicated in patients with AHF associated to pulmonary disease and may be considered, after haemodynamic stabilization, in some patients with CS. There are no differences in the outcomes in the studies comparing both techniques, but CPAP is a simpler technique that may be preferred in low-equipped areas like the pre-hospital setting, while NIPSV may be preferable in patients with significant hypercapnia. The new modality 'high-flow nasal cannula' seems promising in cases of AHF with less severe RF. The correct selection of patients and interfaces, early

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application of the technique, the achievement of a good synchrony between patients and the ventilator avoiding excessive leakage, close monitoring, proactive management, and in some cases mild sedation, may warrant the success of the technique.

## Keywords

Non-invasive ventilation • CPAP • Bilevel pressure support • Acute heart failure • Acute cardiogenic pulmonary oedema • High-flow nasal cannula

## Introduction

Acute respiratory failure (RF), defined as fall in blood oxygen concentration (hypoxaemia) with or without hypercapnia, is one of the most important causes of emergency department presentation in adults. High-flow 'Venturi' masks and low-flow reservoir masks or thin nasal cannulas are the standard forms of conventional oxygen therapy (COT) to treat these patients. However, RF is not often fully compensated with COT and requires greater respiratory support. Traditionally, this was only provided by a ventilator, generating positive intrathoracic pressure (PIP) via endotracheal intubation (EI). Nevertheless, EI carries its own risks, and usually requires complete sedation and admission to a critical care area. Non-invasive ventilation (NIV) is a technique that emerged in the 1980's, that consists of applying positive pressure to conscious patients through different interfaces, it has been shown to be useful in acute RF, reducing the need for EI and decreasing its associated risk of infection, mainly ventilator-associated pneumonia.<sup>1</sup> Since its introduction, NIV has been extended to different areas of the hospital, the pre-hospital setting and even domiciliary care, while ventilation through EI has remained limited to critical units or the operating theatre. Non-invasive ventilation is indicated to treat RF in a range of different scenarios, including dysfunction of the nervous system, muscles, chest wall, airways, and lung parenchyma, such as acute heart failure (AHF).

## Acute respiratory failure in acute heart failure syndromes

Pulmonary oedema is the second most frequent (after pneumonia) acute parenchymal alteration causing RF. Some degree of pulmonary (interstitial/alveolar) oedema may be observed in most of patients with AHF syndromes.<sup>2</sup> Consequently, nearly 90% of AHF patients complain of dyspnoea,<sup>3</sup> but fewer than half present with RF affecting the blood gas analysis, in form of hypoxaemia, hypercapnia, acidosis, or a combination thereof.<sup>4</sup> In relation to the different AHF syndromes, significant RF is primarily seen in acute cardiogenic pulmonary oedema (ACPE), in cardiogenic shock (CS) and in cases associated to other lung alterations.<sup>2,5</sup>

*Acute cardiogenic pulmonary oedema:* The hallmark of this syndrome is a rapid increase in pulmonary capillary hydrostatic pressure and trans-vascular fluid filtration that exceeds the lymphatic interstitial drainage capacity.<sup>6</sup> Respiratory failure occurs when an excess of interstitial and alveoli fluid results in a significant reduction of gas exchange and a concomitant shunt effect. Acute cardiogenic pulmonary oedema is a stressful scenario with progressive RF that may lead to cardiorespiratory collapse in hours, or minutes, unless therapeutic

action is taken. Several clinical criteria are required for the diagnosis of ACPE (Table 1).<sup>7,8</sup> Initial bedside assessment using the clinical criteria allows the initiation of urgent therapies, but the diagnosis should be confirmed thereafter by additional criteria, more specific for AHF. Key clinical findings are respiratory distress and RF. Other AHF scenarios with interstitial or mild alveolar oedema without significant RF or respiratory distress would not be considered ACPE.

The rate and speed of alveolar fluid filtration, microvascular membrane permeability, alteration in sodium-chloride and water reabsorption, as well as inflammation and individual genetic susceptibility

**Table 1** Diagnostic criteria for acute cardiogenic pulmonary oedema

### Clinical criteria (all of them)

- Acute respiratory distress<sup>1</sup>
- Physical examination<sup>2</sup>
- Orthopnoea
- Respiratory failure<sup>3</sup>

### Diagnostic confirmation (at least two of the following)

- Clear signs of pulmonary congestion on chest radiography or CT scan
- Multiple B-lines on lung ultrasound<sup>4</sup>
- Elevated pulmonary capillary pressure on catheterization
- Increased total lung water on pulse contour and thermodilution analysis system
- Signs of elevated filling pressures on echocardiography<sup>5</sup>
- Significant elevation of natriuretic peptides<sup>6</sup>

- (1) Respiratory distress: Acute increase in the work of breathing (assessed by single inspection), significant tachypnea (RR > 25 breaths/min)<sup>a</sup>, may be with the use of accessory muscles or abdominal paradox
- (2) Crackles ± wheezes over the lungs, third heart sound<sup>b</sup>
- (3) Oxygen saturation on room air by pulse-oximetry (SpO<sub>2</sub>) < 90%. Arterial blood gases may also show PaO<sub>2</sub> < 60 mmHg, PaCO<sub>2</sub> > 45 mmHg or PaO<sub>2</sub>/FiO<sub>2</sub> < 300 mmHg
- (4) ≥ 3 B-Lines in two chest zones on each hemithorax<sup>7,8</sup>
- (5) E/E' > 15. Other parameters of elevated left atrial pressure may also be considered
- (6) Natriuretic peptides<sup>c</sup> BNP > 400 or N-ProBNP > 900 (or 1800 in > 75 years)

<sup>a</sup>Respiratory rate may be lower and orthopnoea may be absent in obtunded patients.

<sup>b</sup>Patients with low systolic blood pressure (i.e. < 90 mmHg) may be considered to have cardiogenic shock rather than ACPE.

<sup>c</sup>In 'flash pulmonary oedema' BNP may be lower. RR, respiratory rate; CT, computer tomography.

play an important role in the genesis of this syndrome. Patients with ACPE often present hypertension on admission. Those who have hypertensive ACPE more frequently show preserved left ventricular (LV) ejection fraction (EF), hypercapnia, but they have a lower EI rate and a better prognosis than those with lower blood pressure.<sup>9</sup> Many of them may have a very rapid presentation, commonly termed 'flash ACPE', without previous clinical signs of accumulation of fluids.<sup>10</sup>

**Cardiogenic shock (CS):** When CS is secondary to LV failure, acute RF is nearly always present, with concomitant pulmonary oedema and tissue hypoperfusion. In addition to pulmonary oedema, the reduction in lung perfusion produces an increase in pulmonary dead space (some ventilated areas receive less blood), increasing the ventilation–perfusion mismatch. In addition, systemic circulatory failure precipitates metabolic acidosis (lactic acidemia), that increases the compensatory respiratory load, and reduces central venous oxygen content (SvO<sub>2</sub>) by an augmented arterio-venous difference (greater tissue oxygen extraction). These abnormalities exacerbate the RF in CS.

**Other scenarios:** Patients with AHF often have concomitant COPD, asthma, pneumonia, large pleural effusion, atelectasis or pulmonary embolism, which may precipitate or aggravate RF. Further, in isolated right ventricular (RV) failure, RF is mainly seen in cases of acute pulmonary thrombo-embolism or decompensated chronic pulmonary hypertension.

## Rationale for non-invasive ventilation in acute heart failure

The net effect of PIP is an increase in oxygenation and a decrease in the work of breathing.<sup>11</sup> In the case of ventilatory support, an additional improvement in alveolar ventilation should be expected, with further decreases in the work of breathing and carbon dioxide levels. However, positive pressure changes heart–lung interactions, with haemodynamic and respiratory effects (Table 2), including a tendency to reduce cardiac output and blood pressure. Conversely, in AHF patients with elevated preload and afterload, it may increase cardiac output by reducing both pre- and afterload<sup>12,13</sup> and reducing intrapulmonary shunting.<sup>14</sup> Finally, when there is isolated RV dysfunction, positive pressure may be detrimental as the increase in RV afterload may precipitate or aggravate RV failure.

## Modalities of non-invasive ventilation

Table 3 shows the features of the most commonly used modalities of NIV in acute settings. The main applications are continuous positive airway pressure (CPAP), non-invasive pressure support ventilation (NIPSV), and more recently, high-flow nasal cannula (HFNC).

**Continuous positive airway pressure (CPAP)** is the simplest NIV technique and consists of the application of continuous positive pressure into the lungs (Figure 1). It can be applied without the aid of a ventilator, by using a source of air or oxygen to renew the air through a hermetically sealed mask equipped with positive end expiratory pressure (PEEP) valve, or with the Boussignac system.<sup>15</sup>

**Table 2** Main physiologic effects of positive intrathoracic pressure

Cardiovascular
↓ Venous return → ↓ RV preload → ↓ LV preload
↑ Pulmonary vascular resistance → ↑ RV afterload → RV enlargement → ↓ LV Compliance
↓ LV afterload (↓ systolic wall stress)
↓ Systemic blood pressure → ↓ Cardiac output <sup>a</sup>
Respiratory
Recruitment of collapsed alveoli → ↑ Functional residual capacity
Maintenance continuously opened alveoli → Gas exchange during the whole respiratory cycle
Intra-alveolar pressure against oedema
↓ Work of breathing
↑ Oxygenation

<sup>a</sup>In patients with AHF with elevated LV preload and afterload, cardiac output may increase as consequence of the application of positive intrathoracic pressure. RV, right ventricle; LV, left ventricle.

**Non-invasive pressure support ventilation (NIPSV):** This modality, the core of NIV, requires a ventilator. It is programmed with two levels of pressure: expiratory pressure (EPAP) or PEEP, and inspiratory pressure (IPAP), which is obtained with pressure support (See Figure 2). It is also called non-invasive intermittent positive pressure ventilation (NIPPV), or sometimes bilevel or BiPAP. The final result is equivalent to a CPAP mode with inspiratory assistance. This method requires some experience for setting the ventilator to the changing needs of the patient. Adequate synchrony is essential. The respiratory rate is not pre-set and depends exclusively on the patient.

**High-flow nasal cannula (HFNC):** This system delivers a heated and humidified oxygen–gas mixture (up to 60–80 L/min) that exceeds patients' spontaneous inspiratory demand through a nasal cannula adjusted to the nostrils (Figure 3). There are beneficial actions: a low level of PEEP (<5 cmH<sub>2</sub>O); a washout effect in nasopharyngeal.<sup>16</sup> It should be noted that with an open mouth, the PEEP effect practically disappears.<sup>17</sup> This could be a disadvantage in ACPE patients with severe dyspnoea who generally mouth breath.

**Other modalities:** See Table 3 for explanations.

## Evidence and recommendations for the use of non-invasive ventilation in acute heart failure syndromes

### Continuous positive airway pressure and non-invasive pressure support ventilation in acute cardiogenic pulmonary oedema

Acute cardiogenic pulmonary oedema is the second most frequent indication for NIV.<sup>18</sup> The first randomized trials performed at the end of the 1980's using CPAP, showed faster improvement of RF than COT<sup>19,20</sup> with a reduction in EI rate.<sup>20</sup> The first randomized trial of

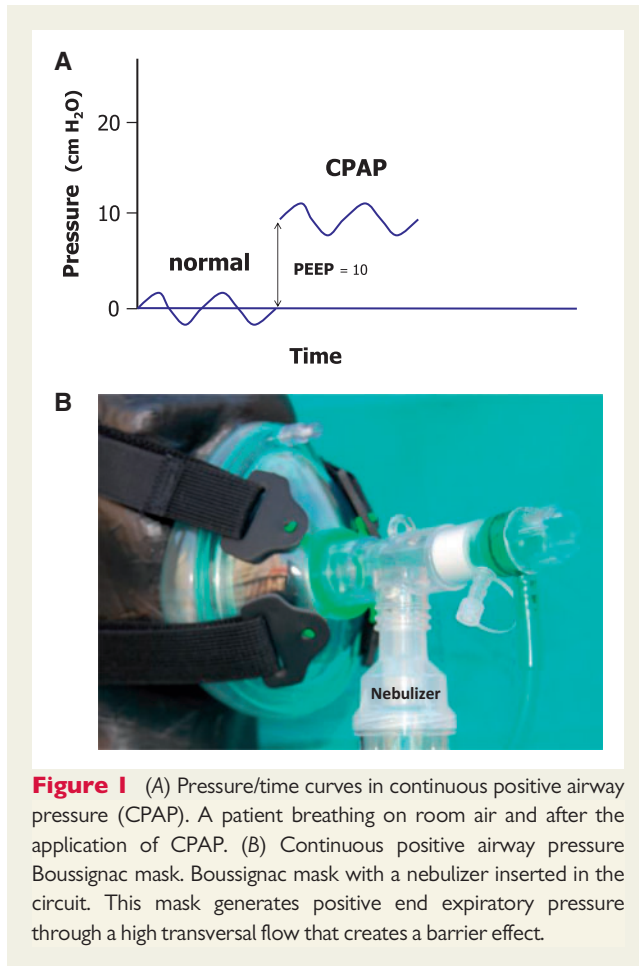
**Table 3** Main modalities of NIV

	Main characteristics	Advantages	Disadvantages	Main indication
CPAP	Continuous positive intra-thoracic pressure	Very simple use Does not require a ventilator Improves oxygenation	Does not provide ventilatory help on inspiration	ACPE Atelectasis Obstructive sleep apnoea
HFNC	High humidified flow (up to 60–80 L/m) through nasal cannula, producing: <ul style="list-style-type: none"> <li>• Low level of PEEP</li> <li>• Decreased upper airway resistance</li> <li>• Tracheal air washout</li> </ul>	Simple use Does not require a ventilator Good adaptation Improves oxygenation	Does not provide ventilatory help on inspiration	Sub-acute ACPE AHF needing prolonged NIV Hypoxaemic respiratory failure Weaning from mechanical ventilation
NIPSV	Inspiration: Decelerated flow to maintain a target pressure (pressure support) triggered by patient's effort. Expiration: PEEP	Provides ventilatory support Results as a continuous positive pressure plus a help on inspiration	Needs expertise and appropriate device. May produce overassistance when patients increase inspiratory effort	ACPE AHF and COPD Hypercapnic respiratory failure Weaning from mechanical ventilation
PAV	Adjusts ventilator assistance to the activity of respiratory muscles estimated by an algorithm, proportionally to the patient's effort	Provides ventilatory support Better adaptation than NIPSV May prevent overassistance	Mismatching in complex respiratory pattern	Potentially indicated in patients with asynchrony with NIPSV It has been used in ACPE
APC-AVAPS	Changes inspiratory pressure to maintain constant a target volume	Provides ventilatory support Ensures minute ventilation	Tidal volume limitation is not guaranteed in higher inspiratory drive High pressures in cases of low lung compliance	COPD encephalopathy Hypoventilation syndrome No indication in AHF
NAVA	Inspiratory support triggered by diaphragm contraction	Earliest trigger and maximal adaptation to patient's inspiratory drive	Requires oesophageal catheter	More commonly used in intubated patients No indication in AHF
ASV	Changes inspiratory pressure and PEEP according to the respiratory pattern of the patient	Provides ventilatory support Ensures minute ventilation and adapted PEEP, avoiding apnoeas	May be harmful in patients with chronic heart failure sleep disorders and low EF	Complex sleep disorders It has been used in ACPE

CPAP, continuous positive airway pressure; NIPSV, non-invasive pressure support ventilation; HFNC, high-flow nasal cannula; PAV, proportional assist ventilation; APC-AVAPS, adaptive-pressure-control (APC) or average volume-assured pressure support; NAVA, neurally adjusted ventilatory assist; ASV, adaptive servoventilation; ACPE, acute cardio-pulmonary oedema; PEEP, positive end expiratory pressure; AHF, acute heart failure; EF, ejection fraction; COPD, chronic obstructive pulmonary disease.

NIPSV in ACPE, published in 2000, showed similar results.<sup>21</sup> Several meta-analyses<sup>22–24</sup> revealed both techniques reduced the EI rate, and tended to reduce mortality as compared to COT, a trend that was statistically significant for CPAP. However, in 2008, a large randomized trial (3-CPO) including 1069 patients with acidotic (pH < 7.35)

ACPE assigned to CPAP, NIPSV, or COT,<sup>25</sup> showed no difference in mortality, although both NIV techniques improved respiratory distress faster than COT. There may be several explanations for the discrepancy between this trial and the prior meta-analyses. The first is the population studied: nearly one-third of the trials included in the



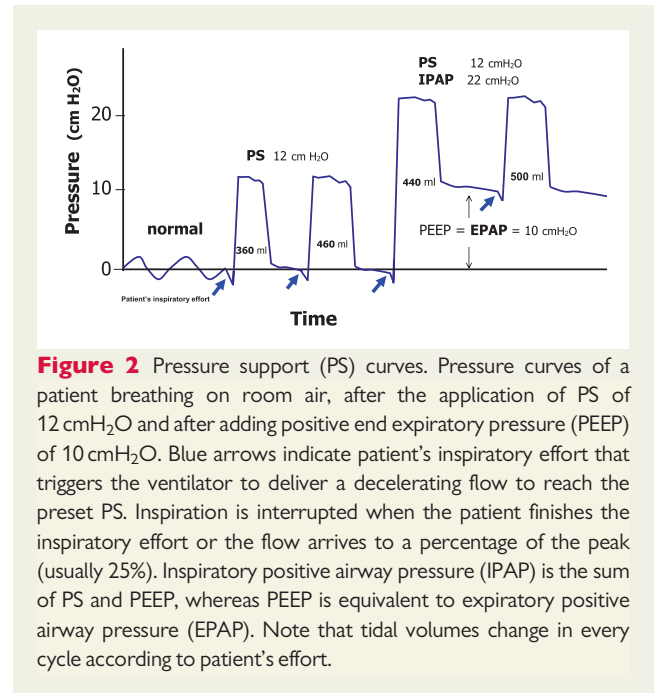
**Figure 1** (A) Pressure/time curves in continuous positive airway pressure (CPAP). A patient breathing on room air and after the application of CPAP. (B) Continuous positive airway pressure Boussignac mask. Boussignac mask with a nebulizer inserted in the circuit. This mask generates positive end expiratory pressure through a high transversal flow that creates a barrier effect.

meta-analyses were performed in ICUs, suggesting that were sicker patients, and in fact, showed higher rates of EI (21.9% vs. 2.9%) and mortality (15.3% vs. 9.6%).<sup>26</sup> In addition, the patients in 3-CPO were not hypoxaemic (mean PaO<sub>2</sub> was 100 mmHg in the three arms at study entry), meaning that a clear advantage from NIV in might not be easily shown in patients with mild RF and very low EI rate. The second argument concerned crossover. There was a high crossover rate in 3-CPO (nearly 20% of the patients) mainly due to discomfort (intolerance) in NIV groups, or worsening RF in the COT group (which was significantly higher than in the NIV groups). Finally, although the effect of NIV on mortality after the 3-CPO remains inconclusive, a subsequent meta-analysis including this trial, showed that both modalities reduced the EI rate and still CPAP reduced mortality [relative risk 0.64 (95% CI, 0.44–0.92)], mainly in high-risk patients with acute coronary syndromes.<sup>27</sup>

There are no specific trials focused on patients with hypertensive ACPE, but in this case, NIV may be used to improve symptoms.<sup>28</sup>

Several studies have shown that the early application of CPAP in the pre-hospital care of patients with ACPE improved RF faster than COT, with a tendency to reduce the EI rate.<sup>29–31</sup> Because CPAP does not require special training or expensive equipment it can be recommended in this setting.

Recent surveys have shown a dramatic expansion in use of NIV in the general population in the last decades, particularly in ACPE,<sup>32</sup> but



**Figure 2** Pressure support (PS) curves. Pressure curves of a patient breathing on room air, after the application of PS of 12 cmH<sub>2</sub>O and after adding positive end expiratory pressure (PEEP) of 10 cmH<sub>2</sub>O. Blue arrows indicate patient's inspiratory effort that triggers the ventilator to deliver a decelerating flow to reach the preset PS. Inspiration is interrupted when the patient finishes the inspiratory effort or the flow arrives to a percentage of the peak (usually 25%). Inspiratory positive airway pressure (IPAP) is the sum of PS and PEEP, whereas PEEP is equivalent to expiratory positive airway pressure (EPAP). Note that tidal volumes change in every cycle according to patient's effort.

with a wide variation among centres.<sup>33</sup> Data from 2430 patients who required ventilatory support in the ADHERE registry, supported the use of NIV to avoid EI.<sup>34</sup>

The latest ESC guidelines have given NIV a Class IIa recommendation with level of evidence B<sup>35,36</sup> in patients with respiratory distress (respiratory rate > 25 breaths/min, SpO<sub>2</sub> < 90%). The NICE guidelines in AHF recommended NIV in patients with ACPE with severe dyspnoea and acidemia.<sup>37</sup> Finally, the very recent guidelines from ERC/ATS recommend NIV, either bilevel NIV or CPAP, for patients with ARF due to ACPE and suggest it in the pre-hospital setting.<sup>38</sup>

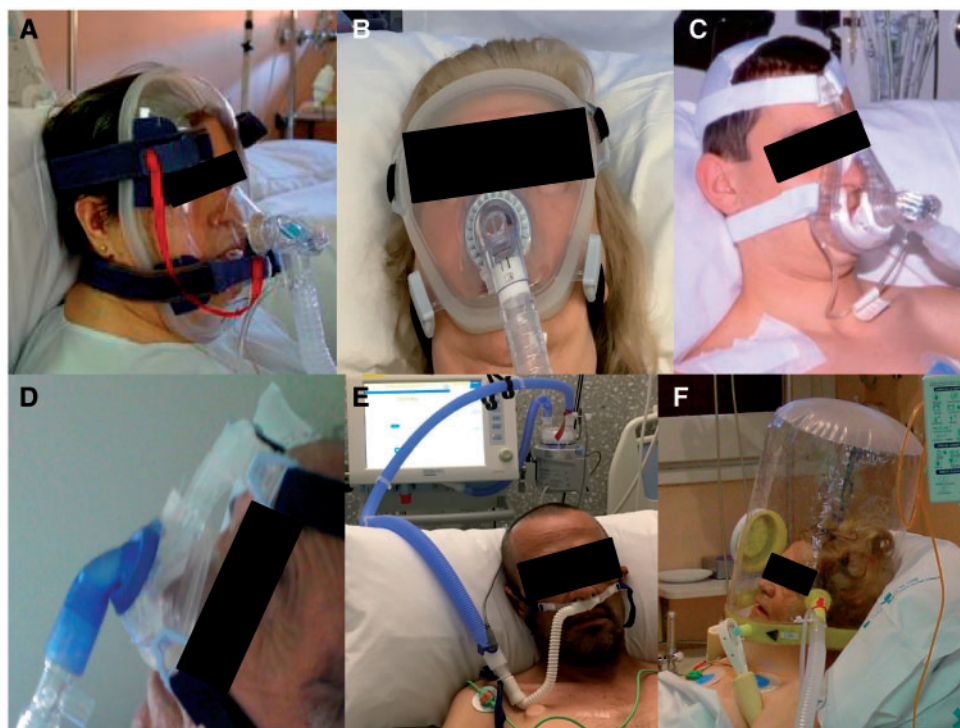
We recommend that NIV should be used in patients with ACPE, as defined above, in order to reverse RF faster, avoid EI and, with lower evidence, potentially reduce mortality in high risk patients. Continuous positive airway pressure may be the best option in the pre-hospital setting.

## High-flow nasal cannula in acute heart failure

In adults, HFNC has recently shown to be effective in the weaning of patients from mechanical ventilation<sup>39,40</sup> and in hypoxaemic RF from different aetiologies.<sup>41</sup>

In AHF the data are scarce, with only one randomized study published this year. This included 128 patients with ACPE, in which HFNC only showed a greater decrease in respiratory rate after 60 min compared to COT.<sup>42</sup> High-flow nasal cannula has been also used in stable Class III heart failure patients<sup>43</sup> and in a short series of AHF patients needing prolonged ventilation support.<sup>44</sup>

In some comparative studies HFNC was better tolerated than NIPSV,<sup>45</sup> which anticipates an expansion of the technique. It can be recommended in patients needing prolonged ventilation support, during weaning and in hypoxaemic AHF not tolerating CPAP/NIPSV or failing COT, although further trials are necessary to establish its optimal indications.<sup>46</sup>



**Figure 3** Main interfaces used in non-invasive ventilation (NIV). (A–B) Two different models of *total-face mask* (probably with the best patient-ventilator adaptation)<sup>69</sup>; (C) *Oronasal mask*: the most used interface; (D) *Nasal mask*: not indicated in patients breathing by the mouth as those with acute pulmonary oedema. (E) *High-flow nasal cannula*: (see text); (F) *Helmet*: mostly used for continuous positive airway pressure mode, it allows more patient autonomy (speaking and eating), convenient when anticipating prolonged NIV. Other interfaces like *nasal pillows*, *mouthpieces* or *laryngeal masks* are usually not considered in acute heart failure.

## Other modalities in acute heart failure

In a small randomized trial including 36 patients, *Proportional Assist Ventilation* showed similar results vs. CPAP.<sup>47</sup> In a series of patients with ACPE from Japan, *Adapted Servoventilation* resulted slightly better than COT.<sup>48</sup> However, this technique showed a potential increase in mortality when was applied to treat sleep apnoea in patients with chronic heart failure and reduced EF<sup>49</sup> and therefore, it was considered Class III in the latest ESC-guidelines.<sup>35</sup> Other modalities<sup>50,51</sup> presented in *Table 3* have not been tested in AHF.

## Non-invasive ventilation and myocardial infarction

Acute myocardial infarction (AMI) is a frequent cause of ACPE. However, the clinical picture may be confusing as ACPE often is associated with a rise in high-sensitivity troponin, and it may be difficult to know whether ACPE was precipitated by AMI or whether cardiomyocyte injury was the consequence of ACPE.<sup>52</sup> Two old studies suggested that NIPSV could precipitate AMI. The first comparing NIPSV to CPAP was prematurely stopped after recruiting 27 patients due to a higher rate of AMI in the NIPSV group,<sup>53</sup> but the majority of patients already had chest pain on admission, suggesting a recruitment bias rather than an effect of ventilatory therapy. The second study, started in mobile intensive care units in Israel,<sup>54</sup> compared NIPSV to nitrates and showed higher rates of AMI (55 vs. 10%) and EI (80% vs. 20%) in

the NIV group. However, patients allocated to the NIV received less intravenous medical therapy and the protocol imposed strict ventilator restrictions, resulting in a very low pressure support (average: 5 cmH<sub>2</sub>O) that could have led to hypoventilation. This may have contributed to the poor results with NIV in this trial, as low tidal volumes may increase alveolar oedema due to the negative intrathoracic pressure precipitated by the patient's inspiratory effort.<sup>55</sup> No other trial has reproduced these results, including randomized trials specifically designed to assess this issue,<sup>56–58</sup> case-control studies<sup>59</sup> or meta-analyses. In addition, in 3-CPO, NIV was safely used in patients with AMI, who accounted for nearly 50% of the population enrolled, with no differences in the incidence of AMI between groups.<sup>25</sup> However, it should be emphasized that patients with ST segment elevation (STEMI) have not usually been included in the trials. On the other hand, recent data have shown no effect of oxygen therapy in patients with suspected AMI without hypoxaemia.<sup>60</sup>

In summary, there is no relationship between use of NIV and risk of AMI, and NIV may be considered in patients with ACPE complicating a Type II AMI or a non-STEMI. Further data are necessary to assess the role of NIV in patients with STEMI.

## Non-invasive ventilation in cardiogenic shock

There are no studies analysing NIV in this clinical situation. Traditionally, patients with CS have not been candidates for the

technique. Although RF is always present in these patients, frequently altered mental status does not ensure correct spontaneous breathing and preservation of the upper airway, two conditions necessary for the appropriate use of NIV. Furthermore, PIP tends to decrease blood pressure, aggravating hypoperfusion. However, in the 'Cardshock study',<sup>61</sup> NIV was used in nearly 13% of the patients with early or non-severe CS, after correction of hypotension, avoiding EI in the majority.<sup>62</sup> Therefore, although the use of NIV remains limited in hypotensive patients, it may be cautiously considered in selected CS patients without severe haemodynamic instability. The potential use of HFNC in this context should be assessed.

## Non-invasive ventilation in other acute heart failure scenarios

There are no randomized studies specifically analysing the effect of NIV in patients with isolated RV failure. As a general rule, mechanical ventilation should be avoided in these patients.<sup>63</sup> However, in cases with RF of mixed origin (COPD with pulmonary oedema), NIV may be especially useful because it may benefit both underlying conditions.<sup>64</sup>

## Continuous positive airway pressure or non-invasive pressure support ventilation

Although theoretically NIPSV should be superior to CPAP because it provides an inspiratory help, no trials or meta-analyses have demonstrated a clear advantage of one technique over the other for important outcomes in patients with AHF, but those treated with NIPSV have shown faster improvement in several physiological variables in some trials.<sup>53,65–67</sup> In case-series of patients with ACPE, NIPSV was most clearly effective in those with hypercapnia.<sup>21,68</sup> Consequently, either technique can be used as a first line treatment in ACPE, but it seems reasonable to prefer NIPSV in patients with severe hypercapnia, although little evidence supports this recommendation.

## Practical aspects

### Equipment

#### Interfaces

The interface is the component that most defines NIV, and it is crucial for treatment success. In order to avoid leaks, a tight seal between the patient's face and the device is essential, but often difficult to obtain. There are different types of interfaces (see *Figure 3*).<sup>69</sup>

#### Ventilators

There are three types of ventilators: portable (designed specifically for NIV), transport, and ICU-ventilators. All of them have particular settings for CPAP and NIPSV.

Portable NIV ventilators are less expensive have higher mobility, do not need an air flow source and seem to allow better synchrony than ICU and transport ventilators.<sup>70</sup> A wide range of ventilators is currently on the market, from the simplest (only pressure is modifiable) to the latest generation high-tech ventilators (display monitoring, alarm setting, leakage compensation, different triggers, cycling and flow ramp control, etc.). The most important attribute of the

**Table 4** Contraindications of NIV

Absolute	Cardiac or respiratory arrest Anatomical abnormality (unable to fit the interface) Inability to keep patent airway (uncontrolled agitation, coma <sup>a</sup> or obtunded mental status) Refractory hypotension
Relative	Mild agitation or poor cooperation Mild hypotension Upper gastrointestinal haemorrhage or vomiting Inability to expectorate copious secretions Recent frail upper gastrointestinal or airway surgery Multiorgan failure Isolated right ventricular failure

<sup>a</sup>Modalities like NIV with volume controlled or 'Average volume assured pressure support' have been used in hypercapnic encephalopathy.

equipment is leakage compensation through an increase of air flow (up to 120–180 L/min).

### Complements

*Skin protectors* are recommended. *Heat humidification or heat and moisture exchangers* are recommended because they may facilitate NIV.<sup>71</sup> *Nebulizers* can be used safely without interrupting NIV therapy.

*Sedation*: Mild sedation decreases respiratory rate and intolerance<sup>72,73</sup> and is used nearly 20% of the patients treated with NIV.<sup>74</sup> However, sedation may cause adverse events (hypoventilation, hypotension and also, vomiting or aspiration with opioids) and should be used only in patients who remain uncooperative or who show poor synchrony with the ventilator, and then only after non-pharmacological approaches have been tried<sup>75</sup> (e.g. changing the interface, tuning the ventilator, reassuring the patient, etc.). Experienced staff and appropriate monitoring (e.g. targeting a sedation scale or respiratory rate) is essential.<sup>76</sup> Minimal intermittent doses of a single drug may be preferable to continuous infusions or combinations of different agents.<sup>74,75</sup> Morphine (boluses of 2–4 mg) is the most used single drug in this setting,<sup>72</sup> although recent data raised safety concern of its use in AHF.<sup>77</sup> Other opioids, propofol, midazolam, and more recently dexmedetomidine, which is an  $\alpha_2$ -adrenergic receptor agonist with less central respiratory depression, have been used in this context.<sup>75,76</sup>

### Starting non-invasive ventilation

Before starting the technique, the contraindications for NIV should be considered (*Table 4*). Empathic communication between nurses/physicians and the patient is essential, with clear instructions about what to expect and frequent encouragement thereafter. By fitting the mask manually at the onset, patients gain confidence with the technique, and it later may be secured fixed with strips in a similar manner.

#### Device settings

For NIPSV, it is recommendable to start with low levels of PEEP (3–4 cmH<sub>2</sub>O) and pressure support of 7–8 cmH<sub>2</sub>O, increasing it progressively according to patients' adaptation and response. Target tidal volumes are 4–7 mL/kg (often lower in COPD patients). With

**Table 5** Monitoring NIV

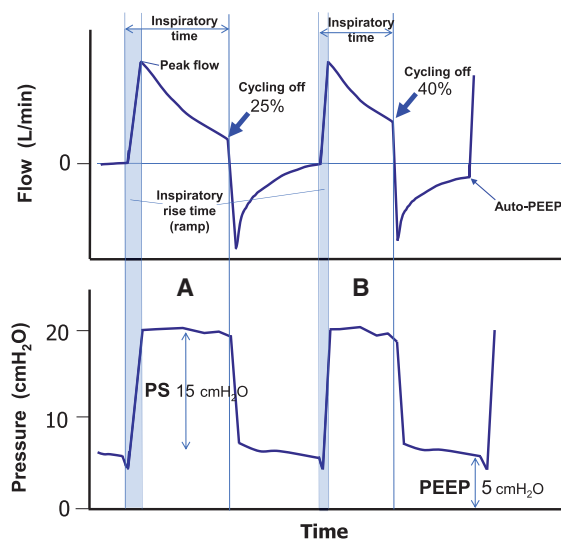
Patient
Respiratory rate
Other vital signs
Dyspnoea/accessory muscle use/abdominal paradoxical breathing
Level of consciousness
Comfort with the interface
Collaboration
Ventilator parameters
Tidal volume (>4 mL/Kg; 6–7 mL/Kg) and minute ventilation
Air leakage volume (<0, 4 L/s or < 25 L/min)
Pressure support and PEEP settings
Asynchrony (ineffective efforts, auto-triggering, double-triggering, short/long cycle) <sup>a</sup>
Trigger/slope (ramp)/Inspiration time/expiration settings
Auto-PEEP
Alarms (apnoea or high respiratory rate, low/high minute ventilation, others)
Gas exchange
Continuous pulse-oximetry (SpO <sub>2</sub> )
Arterial or venous blood gas samples <sup>b</sup>
Risk factors of failure
Before initiation
Lung infection
Altered mental status
Hypotension
High severity scores
Copious secretions
Extremely high respiratory rate
Severe hypoxaemia in spite of high F <sub>I</sub> O <sub>2</sub>
After initiation
Inappropriate ventilator settings
Unfitting interface
Excessive air leakage
Asynchrony with the ventilator
Poor tolerance to NIV
After 60–90 min
No reduction in respiratory rate or carbon dioxide
No improvement in pH or oxygenation (↓SpO <sub>2</sub> or ↓PaO <sub>2</sub> /FiO <sub>2</sub> )
Signs of fatigue
Neurological or underlying disease impairment
Criteria for endotracheal intubation
Cardiac or respiratory arrest
Progressive worsening of altered mental status
Progressive worsening of pH, PaCO <sub>2</sub> , or PaO <sub>2</sub> despite NIV
Progressive signs of fatigue during NIV
Need to protect the airway
Persistent haemodynamic instability
Agitation or intolerance to NIV with progressive respiratory failure

<sup>a</sup>See also Figure 4.

**Asynchrony:** *Ineffective efforts:* inspiratory efforts not followed by a cycled response from the ventilator. *Auto-triggering* or *double-triggering:* cycled respirations out of patients' demand. These asynchronies should be managed by reducing the leakage, tuning the inspiratory trigger, and adjusting the level of pressure support. *Prolonged cycle (delayed cycling off):* cycled mechanical inspiratory time longer than patient's inspiratory time. It may be compensated by reduction of leakage, decrease of pressure support, inspiratory time or ramp, and when available, titration of expiratory trigger. *Auto-PEEP:* air trapping due to a limitation of the expiratory airflow. Observed in COPD and cases with high respiratory frequency. Treated with measures to extend expiratory time and decrease respiratory rate, titrating PEEP (compensate 80% of the auto-PEEP in COPD patients).

<sup>b</sup>Baseline and after 60–90 min of NIV for: PaO<sub>2</sub>/FiO<sub>2</sub>, pH, PaCO<sub>2</sub>, and bicarbonate; venous samples are suitable for pH, bicarbonate, and SvO<sub>2</sub>.

PEEP, positive end-expiratory pressure; PaO<sub>2</sub>, arterial partial oxygen pressure; PaCO<sub>2</sub>, arterial partial carbon dioxide pressure; FiO<sub>2</sub>, fraction of inspired oxygen; SpO<sub>2</sub>, oxygen saturation by pulse-oximetry; NIV, noninvasive ventilation.



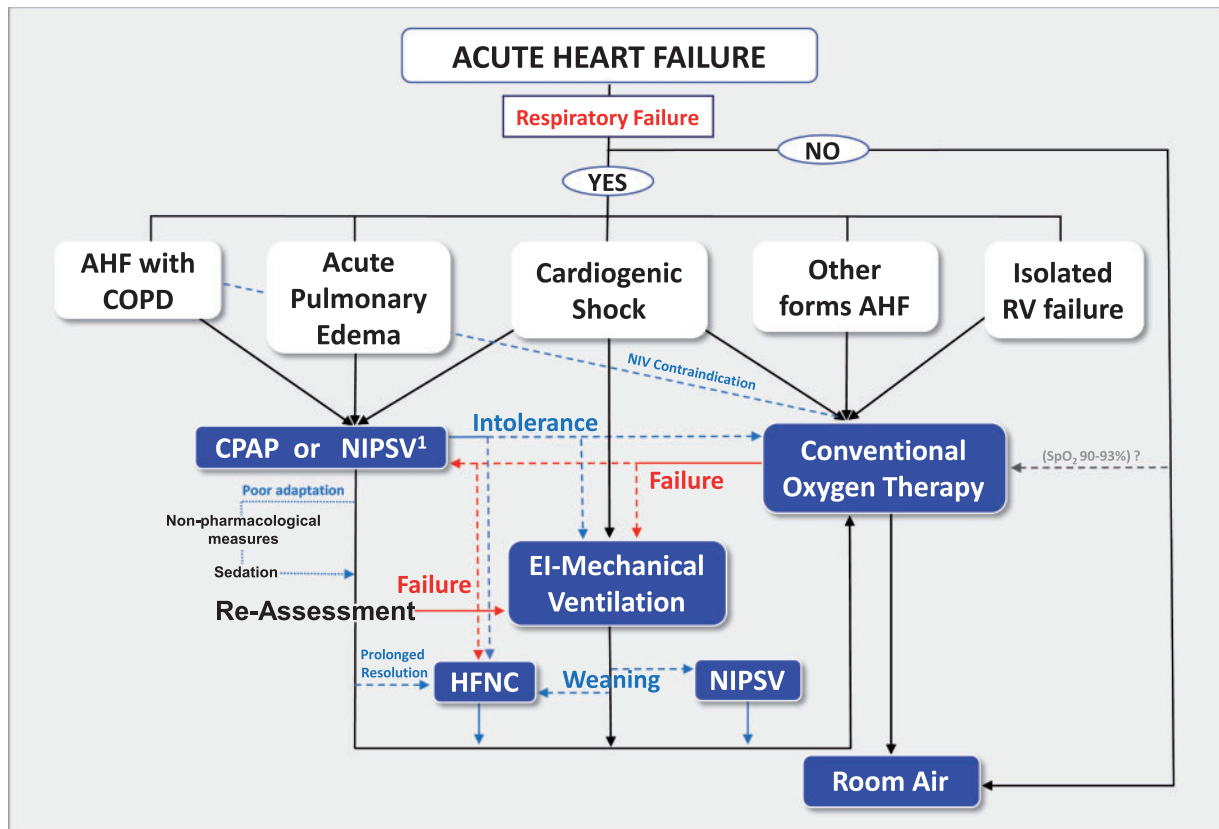
**Figure 4** Pressure and flow curves in non-invasive pressure support ventilation (NIVSV). (A) Non-invasive pressure support ventilation delivered with a cycling off of 25% of the maximal peak flow. (B) Decrease of the inspiratory time after the reduction of the ramp and the increase of the cycling off to 40%. Example of flow curve with Auto-PEEP (the expiratory flow does not arrive to 0). PEEP, positive end expiratory pressure; PS, pressure support.

pressure support of 10–18 cmH<sub>2</sub>O and PEEP of 4–7 cmH<sub>2</sub>O (IPAP 15–20 cmH<sub>2</sub>O/EPAP 4–7 cmH<sub>2</sub>O), a suitable ventilation is generally achieved. High pressures may cause excessive air leakage, asynchrony (especially in patients with high respiratory rate) and discomfort. With portable ventilators, a PEEP over 4 cmH<sub>2</sub>O is usually necessary to avoid rebreathing. F<sub>I</sub>O<sub>2</sub> should be titrated up to 100% to achieve the desired SpO<sub>2</sub>.

When using CPAP, it is advisable to start with 5 cmH<sub>2</sub>O, increasing soon to 7.5 or 10 cmH<sub>2</sub>O, according to the response. When using HFNC in critically ill patients, it is often started with a F<sub>I</sub>O<sub>2</sub> of 100% and the maximum tolerated flow. Later, F<sub>I</sub>O<sub>2</sub> and flow rate can be decreased according to SpO<sub>2</sub><sup>41</sup> and patient's demand. In less severe cases, it is usually started with lower flow and F<sub>I</sub>O<sub>2</sub>.

## Monitoring non-invasive ventilation

To ensure the success of NIV, close monitoring is necessary (Table 5), especially respiratory rate (patient's effort), oxygen saturation (F<sub>I</sub>O<sub>2</sub> may need to be adjusted), and pH/PaCO<sub>2</sub> (to assess efficacy). Visualization of flow and pressure waveforms on a continuous display is recommended<sup>78</sup> (Figure 4). In addition to continuous observation, general reassessment is recommended at 60 and/or 90–120 min, with special attention paid to risk factors for failure.<sup>79</sup> The key issue is optimal synchronization between the patient's spontaneous breathing and the ventilator.<sup>80–82</sup> Air leakage is often involved in cases of asynchrony, which may be reduced by one or more of adjusting the mask, shortening inspiration time, changing



**Take home Figure** Algorithm for non-invasive ventilation in acute heart failure syndromes. After any NIV technique, patients should receive conventional oxygen therapy (COT) before switching to room air. The administration of COT in patients with SpO<sub>2</sub> ranging 91–93% is not clear. <sup>1</sup>Continuous positive airway pressure may be preferred in pre-hospital and low equipped areas, whereas non-invasive pressure support ventilation may be chosen by experienced teams, in patients with significant hypercapnia or COPD. Proportional assist ventilation, adaptive servoventilation, and HFNC have also been used in some trials as first line therapy in ACPE. COPD, chronic obstructive pulmonary disease; HFNC, high-flow nasal cannula; EI, endotracheal intubation; COT, conventional oxygen therapy; ACPE, acute cardiogenic pulmonary oedema.

pressure support by steps of 2 cmH<sub>2</sub>O or moving inspiratory and expiratory triggers (when available) by steps of 5–10% or finally, giving sedation. In general, a leak <0.4 L/s may be tolerated (<25 L/min).

## When to stop

Non-invasive ventilation is usually stopped when a satisfactory recovery has been achieved (usually 2–5 h in ACPE) or conversely, if there are signs of NIV failure, requiring EI (Table 5). After mid- or long-term use of NIV (>24 h), a weaning<sup>83</sup> period is often carried out, by decreasing F<sub>I</sub>O<sub>2</sub>, PEEP, and ventilation settings progressively. Early mobilization may shorten this process. With F<sub>I</sub>O<sub>2</sub> <0.5 and flow rate < 20 L/m, HFNC can be safely replaced by COT.

## Conclusions

In AHF syndromes NIV should be used in patients with ACPE. It may be considered in other AHF patients with RF associated with lung disease and in some cases of CS, after stabilizing the blood pressure. Continuous positive airway pressure is a simpler technique that is

recommended as first line therapy in these scenarios, particularly in the pre-hospital setting or in less well-equipped areas. Non-invasive pressure support ventilation is equally effective in ACPE and may be preferable, by experienced teams, in patients with significant hypercapnia. High-flow nasal cannula may be an alternative, especially in patients with AHF requiring prolonged NIV, but is a well-tolerated NIV technique with wider potential indications.

The overall approach for the use of NIV in AHF, as a complement to recent ESC consensus papers and guidelines,<sup>35,84–86</sup> is shown in *Take home Figure*.

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