REVIEW

Noninvasive positive pressure ventilation in the acute care setting: where are we?

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ABSTRACT: **Noninvasive positive pressure ventilation (NPPV) is a technique used to deliver mechanical ventilation that is increasingly utilised in acute and chronic conditions. The present review examines the evidence supporting the use of NPPV in acute respiratory failure (ARF) due to different conditions.**

Strong evidence supports the use of NPPV for ARF to prevent endotracheal intubation (ETI), as well as to facilitate extubation in patients with acute exacerbations of chronic obstructive pulmonary disease and to avoid ETI in acute cardiogenic pulmonary oedema, and in immunocompromised patients. Weaker evidence supports the use of NPPV for patients with ARF due to asthma exacerbations, with post-operative or post-extubation ARF, pneumonia, acute lung injury, acute respiratory distress syndrome, or during bronchoscopy. NPPV should be applied under close clinical and physiological monitoring for signs of treatment failure and, in such cases, ETI should be promptly available. A trained team, careful patient selection and optimal choice of devices can optimise outcome of NPPV.

Noninvasive positive pressure ventilation is increasingly being used in the management of acute respiratory failure but caregivers must respect evidence-supported indications and avoid contraidincations. Additionally, the technique must be applied in the appropriate location by a trained team in order to avoid disappointing results.

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When the cause of acute respiratory failure (ARF) is reversible, medical treatment works to maximise lung function and reverse the precipitating cause, whereas the aim of ventilatory support is to "gain time" by unloading respiratory muscles, increasing ventilation and thus reducing dyspnoea and respiratory rate, and improving arterial oxygenation and, eventually, hypercapnia and related respiratory acidosis [1]. Most of the complications of invasive mechanical ventilation (table 1) are related to endotracheal intubation (ETI) or to the placement of a tracheostomy tube, to baro- or volutrauma and to the loss of airway defence mechanisms; some others may follow extubation or complicate long-term tracheostomy [2]. Noninvasive mechanical ventilation may avoid most of these complications, ensuring at the same time a similar degree of efficacy [3]. Ventilation-acquired pneumonia (VAP) and other nosocomial infections are reduced by noninvasive ventilation by preserving airway defence mechanisms, owing to the lower requirement for invasive monitoring [4, 5]. This modality enhances patient's comfort, allowing for eating, drinking, cough and communication, avoiding or reducing the need for sedation without an increase in cost and nurse workload compared with invasive mechanical ventilation [6]. In addition, chest physiotherapy can be sufficiently applied. Many devices have been used in the past to deliver noninvasive mechanical ventilation: negative-pressure ventilators, iron lungs, pneumobelts and rocking beds, but in recent years there has been a prevalent, if not exclusive, use of noninvasive positive pressure ventilation (NPPV) [7].

Although continuous positive airway pressure (CPAP) is not considered as a form of ventilation since no inspiratory aid is applied, according to the International Consensus Conference 2001 (Paris, France) [8], NPPV is defined as any form of ventilatory support applied without ETI, and is considered to include: CPAP, with or without

TABLE 1	Complications of invasive mechanical ventilation

Related to tube insertion
 Aspiration of gastric contents
 Trauma of teeth, pharynx, oesophagus, larynx, trachea
 Sinusitis (nasotracheal intubation)
 Need for sedation
Related to mechanical ventilation
 Arrhythmias and hypotension
 Barotrauma
Related to tracheostomy
 Haemorrhage
 Trauma of trachea and oesophagus
 False lumen intubation
 Stomal infections and mediastinitis
 Tracheomalacia, tracheal stenoses and granulation tissue formation
 Tracheo-oesophageal or tracheoarterial fistulas
Caused by loss of airway defence mechanisms
 Airway colonisation with Gram-negative bacteria
 Pneumonia
Occurring after removal of the endotracheal tube
 Hoarseness, sore throat, cough and sputum
 Haemoptysis
 Vocal cord dysfunction and laryngeal swelling

inspiratory pressure support; volume- and pressure-cycled systems; proportional assist ventilation (PAV); and the use of helium–oxygen (heliox) gas mixtures.

NPPV is one of the most important developments in pulmonology over the past 15 yrs [9]. The increasing interest in this topic is clear from the increasing number of published papers over time (fig. 1); research of literature published in the period 1983–2007 (keywords: non invasive mechanical ventilation; non invasive mechanical ventilation and acute respiratory failure) found 1,024 (233 reviews) and 269 (83 reviews) references, respectively. Indeed, a study in 349 intensive care units in 23 countries describing current mechanical ventilation practices and assessing the influence of interval randomised trials when compared with findings from a 1998 cohort found that the use of NPPV increased in 2004 (11.1 *versus* 4.4%) [10]. The present review will focus on recent developments in the application of NPPV in the treatment of acute and acute-on-chronic respiratory failure.

Different conditions leading to acute or acute-on-chronic respiratory failure have been treated with NPPV, but only a few are supported by strong evidence, as follows: prevention of ETI in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) or acute cardiogenic pulmonary oedema (CPO); in immunocompromised patients; as a means of weaning from invasive mechanical ventilation in patients with AECOPD who undergo ETI. Weaker evidence supports the use of NPPV: for patients with post-operative or post-extubation ARF; for patients with ARF due to asthma exacerbations, pneumonia, acute lung injury (ALI) or acute respiratory distress syndrome (ARDS); during bronchoscopy; or as a means of pre-oxygenation before ETI in critically ill patients with severe hypoxaemia (table 2) [11]. The goals of

NPPV may be different according to the underlying pathologies. During AECOPD or acute asthma, the goal is to reduce hypercapnia by unloading the respiratory muscles and increasing alveolar ventilation, thereby improving respiratory acidosis until the underlying problem can be reversed. In acute CPO, the goal of NPPV is to improve oxygenation, reduce the work of breathing and increase cardiac output. During hypoxaemic ARF, the goal is to ensure adequate arterial oxygen tension (Pa,O$_2$) [7].

ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Several prospective, randomised controlled trial (RCTs) [12–19], systematic reviews and meta-analyses [20–22] show a good level of evidence for the clinical efficacy of NPPV in the treatment of acute-on-chronic respiratory failure due to AECOPD. Compared with standard medical therapy alone, NPPV improved survival, reduced the need for ETI and the rate of complications, and shortened the hospital and intensive care unit (ICU) length of stay. Based on these observations, NPPV has been proposed as the first-line ventilatory strategy in this condition with different timing and location according to the level of ARF severity (fig. 2) [23, 24].

Severity of ARF

In patients with ''mild'' AECOPD without respiratory acidosis (pH >7.35), NPPV did not prove to be more effective than standard medical therapy in preventing the occurrence of ARF, and in improving mortality and length of hospitalisation. Furthermore, >50% of the patients did not tolerate NPPV [13, 25]. In patients with mild-to-moderate ARF, as indicated by pH levels 7.30–7.35, NPPV was successfully administered in different settings, including on the ward, in order to prevent ETI [18]. In more severely ill patients (pH <7.25), the rate of NPPV failure was inversely related to the severity of respiratory acidosis, rising to 52–62% [15, 17]. The use of NPPV as an alternative to ETI did not affect the mortality rate and the duration of ventilatory support, but the patients treated with NPPV experienced a lower rate of complications (VAP, difficult weaning). Even in severe patients, although exposed to higher risk of failure, an NPPV trial may be justified if ETI is not strictly required due to the need of protecting the airways and preventing loss of consciousness or gasping [15, 17, 19], provided that facilities for ETI are promptly available.

Severe encephalopathy was considered a contraindication to NPPV based on the concern that a depressed sensorium would predispose the patient to aspiration [3]. More recently, some observations of effective ('' not harmful'') NPPV use in patients with altered levels of consciousness due to hypercapnic ARF were reported [26, 27]. In a recent prospective case–control multicentre study of patients with AECOPD and moderate-to-severe hypercapnic encephalopathy, the use of NPPV *versus* conventional (invasive) mechanical ventilation (CMV) was associated with similar short- and long-term survivals, fewer nosocomial infections and shorter durations of mechanical ventilation and hospitalisation in the subgroup of patients treated successfully with NPPV [28]. SCALA *et al.* [28] suggested an initial cautious NPPV trial in patients with AECOPD and hypercapnic encephalopathy, as long as there are no other contraindications and the technique is administered by an
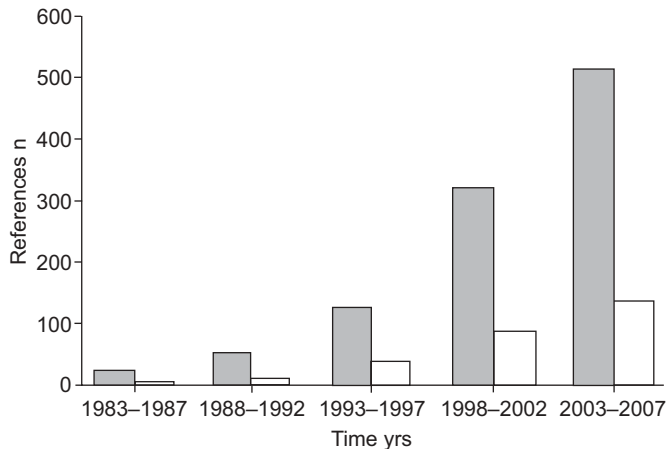
FIGURE 1. Time course of published references on noninvasive (NIV) mechanical ventilation (■), and NIV mechanical ventilation and acute respiratory failure (□). Source: PubMed. Update: December, 2007.

experienced team in a closely monitored setting where ETI is always readily available. Despite this enthusiasm, the current authors feel that larger RCTs, which compare NPPV with CMV among patients with AECOPD presenting with different levels of consciousness and managed in a similar setting, are necessary before these observations translate into routine management.

ASTHMA
In contrast to AECOPD, the use of NPPV in severe exacerbations of asthma leading to ARF is supported by less evidence. MEDURI *et al.* [29] reported successful use of NPPV in 17 episodes of status asthmaticus. Mean pH was 7.25, confirming severe ARF, and NPPV resulted in a rapid improvement in physiological variables; only two patients required ETI. A retrospective noncontrolled study reported favourable outcomes in 22 patients with status asthmaticus treated with NPPV due to persistent hypercapnia [30]. Two other RCTs have reported inconclusive results [31, 32]. As a result of the small sample size of these studies, a recent Cochrane analysis concluded that evidence for use of NPPV in acute asthma was ''promising'' but ''controversial'' [33]. According to the British Thoracic Society Standards of Care Committee Statements: ''NPPV should not be used routinely in acute asthma, but a trial might be considered in patients not promptly responding to standard treatments''[34].

HYPOXAEMIC ACUTE RESPIRATORY FAILURE
Several non-chronic obstructive pulmonary disease (COPD) diseases may lead to hypoxaemic ARF, which is defined by a Pa,O_2/oxygen inspiratory fraction (FI,O_2) ratio $\leqslant 300$ mmHg. This condition is a greater challenge than AECOPD for treatment with NPPV. A recent prospective survey conducted in 70 French ICUs highlighted a possible increase in mortality rate in the subgroup of patients with *de novo* hypoxaemic ARF not related to acute CPO or AECOPD and treated with NPPV, perhaps due to delayed ETI [35]. Owing to the very large spectrum of causes, results of studies on hypoxaemic ARF are difficult to apply to individual patients as frequent failure in a subset of patients may obscure success in another [36].

Therefore, the following subsets of patients will be considered: acute cardiogenic pulmonary oedema; pneumonia; acute lung injury/acute respiratory distress syndrome; and post-operative respiratory failure.

Acute cardiogenic pulmonary oedema
The use of NPPV in acute CPO is supported by RCTs [37–47] and meta-analyses [48–52]. Both mask CPAP and NPPV (inspiratory combined with positive end-expiratory pressure (PEEP); so-called bi-level ventilation) reduce ETI rate and, with a lower level of evidence, mortality rate, compared with standard medical therapy and oxygen. CPAP resulted in easier and less expensive application, and a meta-analysis suggests a greater efficacy in reducing mortality for this modality [51]. However, some studies [38, 39] suggest that NPPV may be preferable for patients with persisting dyspnoea or hypercapnia after initiation of CPAP, whereas early concerns about possible greater risks of myocardial infarction with NPPV [38] were not confirmed [53]. The main physiological benefit of CPAP in these patients is related to decreased left ventricular pre-load and afterload owing to increased intrathoracic pressure, resulting in improved cardiac performance; an increase in functional residual capacity reopens collapsed alveoli and improves oxygenation. This also reduces work of breathing [54].

Pneumonia
NPPV seems disappointing in ARF owing to pneumonia [55, 56], showing failure rates of up to 66% in patients with severe community-acquired pneumonia (CAP) [57]. An RCT of patients with severe CAP showed that NPPV reduced ETI rates, ICU length of stay and 2-month mortality rate, but only in the subgroup with underlying COPD [58]. Another RCT of patients with hypoxaemic ARF [59] showed that NPPV reduced the need for ETI among patients with pneumonia, but a more recent RCT [60], in which NPPV was used as an alternative to ETI in patients with various types of ARF, found that in the subgroup with pneumonia the technique was very unsuccessful. These data do not support the routine use of NPPV in patients with severe pneumonia. However, a cautious trial of NPPV may be considered in patients with pneumonia and underlying COPD under careful monitoring and in the appropriate setting.

Due to the risk of leakage from the mask interface, with subsequent transmission of severe acute respiratory syndrome to healthcare workers, the use of NPPV in such patients requiring mechanical ventilation was not recommended [61]. Nevertheless, promising results with NPPV in this condition have been reported in two studies [62, 63].

Acute lung injury/acute respiratory distress syndrome
The effectiveness of NPPV in the treatment of ALI/ARDS has been investigated by few studies [59, 64]. The mechanism of action of NPPV in ALI/ARDS has been evaluated in a physiological study [65]. Mask pressure support combined with PEEP is needed to unload inspiratory muscles, whereas in this setting CPAP alone improves oxygenation but fails to unload the respiratory muscles. Studies of NPPV for the treatment of ALI/ARDS have reported failure rates ranging 50–80%, but no RCTs have focused on ALI/ARDS exclusively. Independent risk factors for NPPV failure in this group of

TABLE 2	Effectiveness and appropriate location for noninvasive positive pressure ventilation in acute respiratory failure (ARF) from different causes	
Cause of ARF	**Level of evidence[#]**	**Location**
AECOPD	A	Ward, RIICU, ICU
		Depending on severity
Weaning (AECOPD)	A	ICU, RIICU
CPO	A	ICU, RIICU
Immunocompromised patient	A	ICU, RIICU
Post-operative respiratory failure	B	ICU
Pre-intubation oxygenation	B	ICU
Endoscopy	B	Depending on severity
Asthma exacerbations	C	ICU, RIICU
ALI/ARDS	C	ICU
Extubation failure	C	ICU
Do-not-intubate status	C	Ward, RIICU
Pneumonia	C	ICU, RIICU

Evidence A: multiple randomised controlled trials and meta-analyses; evidence B: more than one randomised controlled trial, case–control series or cohort studies evidence; C: case series or conflicting data. AECOPD: acute exacerbation of chronic obstructive pulmonary disease; RIICU: respiratory intermediate intensive care unit; ICU: intensive care unit; CPO: cardiogenic pulmonary oedema; ALI: acute lung injury; ARDS: acute respiratory distress syndrome. [#]: according to [11].

patients include severe hypoxaemia, shock and metabolic acidosis [64]. A recent meta-analysis reported no reduction in the ETI rate and ICU mortality rate with the addition of NPPV to standard care [66]. Conclusions are difficult to draw owing to the heterogeneity of the studies analysed. A recent multi-centre European survey reported the application of NPPV as a first-line intervention in patients with early ARDS, describing what happens in everyday clinical practice in three European ICUs having expertise with NPPV [67]. The technique improved gas exchange and avoided ETI in 54% of patients. Avoidance of ETI was associated with less VAP and a lower ICU mortality rate. Need for ETI was more likely in older patients, with a higher Simplified Acute Physiology Score (SAPS) II and severe hypoxaemia, or when a higher level of PEEP and pressure support was needed [67]. NPPV cannot be recommended as routine therapy for ALI/ARDS. A cautious trial in highly selected patients with less severe general conditions can be attempted in an appropriate location. The use of NPPV should not delay ETI, in case of further deterioration or failure to improve [68].

Post-operative respiratory failure
Both CPAP and NPPV have been successfully used in the post-operative period [69]. Compared with standard treatment, noninvasive CPAP used after major abdominal surgery or thoracoabdominal aneurysm repair improves hypoxaemia and reduces the incidence of complications, such as pneumonia, atelectasis and the need for ETI [70, 71]. Patients with hypoxaemic ARF after lung resection needed less ETI and showed reduced mortality rates if treated with NPPV compared with standard management [72]. Despite there being few studies that have examined different techniques following various surgeries, NPPV should be considered to be among the recommended options for post-surgical patients.

NPPV can play an important role in preventing post-operative pulmonary complications in high-risk patients using chronic ventilators as a consequence of restrictive lung pathology [73].

TRANSPLANTATION AND IMMUNOCOMPROMISED PATIENTS
A small, single-centre study [74] showed that NPPV also has a role in ARF after solid organ transplantation (liver, lung, renal). RCTs in transplant recipients with haematological diseases and hypoxaemic ARF have shown decreased ETI and ICU mortality rates and shorter ICU lengths of stay in patients treated with NPPV as compared with conventional therapy [75]. An RCT in patients with ARF and immunosuppression from various causes reported lower mortality and ETI rates in the subgroup
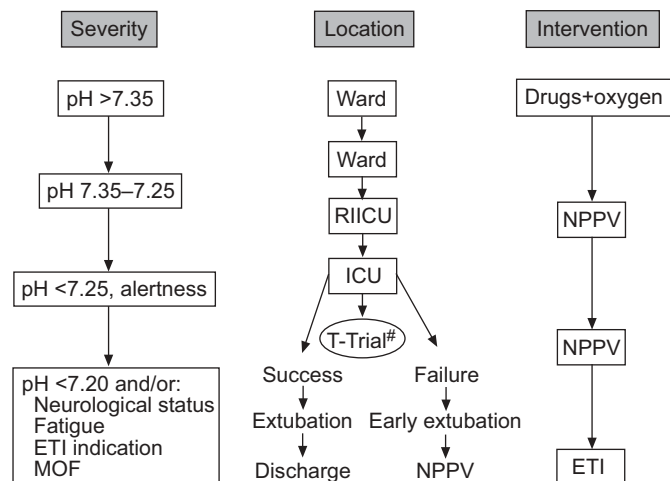

FIGURE 2. Flow chart of the application of noninvasive positive pressure ventilation (NPPV) in acute exacerbations of chronic obstructive pulmonary disease, according to the severity of acute respiratory failure. RIICU: respiratory intermediate intensive care unit; ICU: intensive care unit; ETI: endotracheal intubation; MOF: multiple organ failure. [#]: as described in [81].

of patients treated with NPPV compared with standard treatment. The reduction in mortality was mainly related to the reduction in ETI rate and in the risk of VAP [76]. Similar findings have been reported by a nonrandomised study in patients with AIDS [77]. The reduced mortality rate is likely to be related to reduced infectious complications associated with NPPV compared with ETI, including VAP, other nosocomial infections and septic shock [78]. These findings support NPPV as the preferred initial ventilatory modality for these patients to avoid ETI and its associated risks.

WEANING FROM INVASIVE MECHANICAL VENTILATION IN PATIENTS WITH AECOPD
NPPV has been proposed as a means of facilitating weaning from invasive mechanical ventilation in patients with AECOPD and acute on chronic respiratory failure failing a single [79, 80] or repeated T-piece trial [81]. In extubated patients who were switched to NPPV and weaned according to a standard protocol using pressure support ventilation, RCTs showed increased weaning rates, decreased duration of mechanical ventilation and ICU stay, and reduced rates of VAP compared with CMV. A meta-analysis of studies comparing ''usual'' weaning strategies to early extubation with immediate application of NPPV, confirmed that switch to NPPV resulted in a favourable outcome, including lower mortality rate, lower rate of VAP and shorter total time of mechanical ventilation [82]. The physiopathological basis underlying these results is that NPPV is as capable as invasive ventilation for unloading respiratory muscles and improving gas exchanges; however, this can only partially explain the success of this technique in weaning [83]. Based on these findings, patients intubated for hypercapnic ARF due to AECOPD who fail spontaneous breathing trials should be considered for a trial of extubation to NPPV.

POST-EXTUBATION RESPIRATORY FAILURE
NPPV to treat post-extubation failure
Extubation failure is associated with high morbidity and mortality. Despite a promising previous case–control study in hypercapnic patients [84], an RCT found no reduction in re-intubations among patients who developed ARF within 48 h of extubation [85]. In an RCT evaluating the use of NPPV (compared with standard therapy), as soon as patients (10% with COPD) developed signs of respiratory distress [86], NPPV failed to reduce re-intubations and resulted in increased ICU mortality, possibly related to delays in re-intubation. These findings do not support the use of NPPV as a means of treatment of respiratory failure after extubation. The promising results in hypercapnic patients reported in a previous study [84] need confirmation since there would be still a rationale for using NPPV in this subset of patients.

NPPV to prevent post-extubation failure
Two other RCTs [87, 88] carried out on patients at high risk for extubation failure found that NPPV, applied immediately after extubation, prevented ARF and reduced the need for re-intubation and ICU mortality, with the subset of COPD patients showing the most benefit [88]. NPPV has also been successfully used for the prevention of ARF in the first 48 h post-extubation in severely obese patients [89]. These data support the use of NPPV as a means of prevention of ARF in patients at high risk of extubation failure, in selected patients

and in appropriate settings allowing for strict monitoring and prompt ETI. Routine use in all patients is discouraged [90].

DO-NOT-INTUBATE PATIENTS
NPPV is being increasingly used as an alternative to invasive ventilation in end-stage symptomatic patients [91–95]. A recent European survey in respiratory intermediate intensive care units (RIICU) has shown that NPPV was used as the ceiling of ventilatory care in almost a third of the patients [96]. Clinical trials have recently underlined and confirmed [97, 98] the role of NPPV as an effective alternative to ETI in patients with chronic disease and poor life expectancy (with or without COPD), showing that this ventilatory technique may favourably reduce dyspnoea shortly after initiation even without an associated episode of hypercapnic ARF. The Society of Critical Care Medicine recently initiated a Task Force to develop an approach for considering the use of NPPV for patients who choose to forego ETI [99]. The use of NPPV for patients with ARF could be classified into three categories: 1) NPPV as life support with no pre-set limitations on life-sustaining treatments; 2) NPPV as life support when patients and families have decided to forego ETI; and 3) NPPV as a palliative measure when patients and families have chosen to forego all life support, receiving comfort measures only. The Task Force suggested an approach to use NPPV for patients and families who choose to forego ETI. NPPV should be applied after careful discussion of the goals of care, with explicit parameters for success and failure, by experienced personnel, and in appropriate healthcare settings [99].

The use of NPPV in these extreme circumstances should bear in mind ethical, legal and religious issues. A Spanish study concluded that the use of NPPV offers very low expectations in medium-term survival in do-not-intubate (DNI) patients. The main reason may be that in a country with little experience in advanced directives, the DNI statement coincides with the final stages of disease progression [100].

FIBREOPTIC BRONCHOSCOPY
Confirming a previous preliminary study [101], an RCT has shown that in severe hypoxaemic patients mask CPAP reduces the risk of ARF following bronchoscopy [102]. Another RCT in hypoxaemic patients undergoing bronchoscopy showed that NPPV increased Pa,O_2/FI,O_2, whereas patients randomised to conventional oxygen therapy suffered from a worsening in oxygenation [103]. NPPV has also been reported to be useful in performing successful bronchoscopy in hypercapnic COPD patients with pneumonia [104]. Flexible bronchoscopy in spontaneously breathing young children was associated with significant decreases in tidal volume and respiratory flow, which were reversed by CPAP [105]. The use of NPPV during fibreoptic bronchoscopy is supported by previous evidence and should be considered for use, especially when risks of ETI are high, such as in immunocompromised patients. However, besides competency in endoscopy and in NPPV use, an expert team should be offered the availability of emergent intervention.

SUCCESSFUL NPPV
Successful use of NPPV in ARF depends on several factors, some of which are listed hereafter in order of importance according to the present authors' experience.

Clinical conditions

As in all fields of medicine, the selection of appropriate patients (evidence supported indications) no contraindications, is key to the successful application of NPPV. Most of the contraindications to NPPV listed in table 3 are derived from exclusion criteria for the RCTs. Therefore, it is more correct to state that NPPV is not proven in these circumstances [106]. The use of predictive factors may be useful in the choice of this modality, although, at the end, clinical judgment is important for decision-making. An improvement in arterial blood gases and in sensorium, as assessed by means of the KELLY and MATTHAY score [107], the Glasgow Coma Scale, or the response of a combination of several clinical and physiological parameters to NPPV after the first 1–2 h of NPPV, are used as predictors of success or failure in COPD patients [108–110]. Failure of predictors, as well as presence of contraindications, as listed in table 3, may be considered as criteria for discontinuation of NPPV and intubation or re-intubation. Another issue in the success/failure probability is represented by airway colonisation by nonfermenting Gram-negative bacilli, which is strongly associated with NPPV failure [111]. Nevertheless, even when initially successful, COPD patients with severe ARF treated with NPPV, particularly those with more severe functional impairment during the stable state, may have a late worsening (after >48 h), often requiring ETI, despite an initial brief improvement [112]. Even more difficult is the prediction of NPPV success/failure in hypoxaemic ARF. Predictors of failure were considered to be a SAPS II <34 and $P_{a,O_2}/F_{I,O_2}$ <175 mmHg after the first hour of NPPV in ALI/ARDS [68]. In general, NPPV is more likely to also be successful in different conditions leading to hypoxaemic ARF when hypercapnia is present [11].

Trained team

As in all fields of therapy, NPPV application also follows a learning curve. It has been reported that as caregivers become more confident with NPPV, success rates remain stable despite increasing severity of ARF [113]. A retrospective cohort study in 26 French medical ICUs [114] found that training in NPPV implementation may be an important factor in improving survival and reducing nosocomial infections in critical patients with AECOPD or CPO. Rather interestingly, JOLLIET et al. [57] also reported 10 yrs later that NPPV was not as time consuming as previously reported in 1991 [115].

TABLE 3	Reported contraindications for noninvasive ventilation

Cardiac or respiratory arrest
Severe encephalopathy
Severe gastrointestinal bleeding
Severe haemodynamic instability with or without unstable cardiac angina
Facial surgery or trauma
Upper airway obstruction
Inability to protect the airway and/or high risk of aspiration
Inability to clear secretions

Monitoring and location

Close monitoring is crucial, especially during the initial period of NPPV (table 4). The main concepts for adequate monitoring of patients under NPPV can be summarised by: strict nurse supervision of respiratory and neurological conditions of the patient; noninvasive monitoring of oxygen saturation, cardiac frequency or electrocardiogram and blood pressure; and preference for ventilators with availability of monitoring airway pressures, expired volume and airflow. The problem of monitoring is strictly related to NPPV location, which can actually determine NPPV outcome. Treating a severe hypoxaemia with or without hypercapnia might be even more dangerous in a general ward, whereas it is safer in a monitored high-technology setting, such as in an ICU. In other words, the selection of patients must take into account the location available in which to perform NPPV (table 2; fig. 2) [116]. Several RCTs support the effectiveness of NPPV in the ICU, the RIICU, the general ward and the emergency department [117]. Despite the demonstrated success of NPPV, at least in some clinical conditions, the utilisation rates for NPPV vary enormously among different acute care hospitals within the same region [118]. The perceived reasons for lower utilisation rates reported in the study [118] included lack of physician knowledge, insufficient respiratory therapist training and inadequate equipment. In a survey of NPPV practice in Ontario, Canada [119], the two most common indications for NPPV use were COPD and congestive heart failure. NPPV guidelines, protocols or policies were available in 12 out of 15 hospitals. There was variation in NPPV utilisation among specialties but not hospitals. Specialty (critical care and respirology versus internal and emergency medicine), fewer years of postgraduate experience and a greater number of noninvasive ventilators were predictors of more frequent NPPV use. Only 6% of respondents reported initiation of use and continued use most frequently in non-monitored settings, which increased with the number of noninvasive ventilators. Physician characteristics, such as awareness of the literature, were predictive of NPPV use for AECOPD, whereas perceived NPPV efficacy was predictive of use for many indications, including congestive heart failure. Recently, a case series also reported effectiveness of the NPPV treatment in patients with moderate-to-severe ARF (pH <7.25) as a result of AECOPD in general ward settings [120]. Given the prevalence of patients presenting with severe respiratory acidosis, further studies are needed to better outline the role of NPPV in non-ICU settings.

Interface

The interface is one of the crucial issues affecting NPPV outcome; poor mask tolerance, skin lesions and leaks are reported to be among factors causing NPPV failure and the need for ETI [11]. Although the face mask is usually considered the first choice interface for delivering NPPV in the acute setting, nasal masks were reported to have similar success rates but higher tolerability than oro-nasal techniques in ARF [121]. More recently, a helmet has been introduced to deliver NPPV, reducing discomfort, pressure necrosis of the skin, eye irritation and gastric distension. Some mechanical characteristics of the helmets, which are primarily large volume and highly compliant soft collar compared with the face masks, might, however, impair patient–ventilator interaction. In normal volunteers, during helmet NPPV application, an

TABLE 4	Suggested minimum monitoring of noninvasive positive pressure ventilation during acute respiratory failure
Target	**Tool**
Clinical	
Sensorium	Kelly and Matthay [107] scale, Glasgow Coma Scale
Dyspnoea	Borg Scale, Visual Analogue Scale
Respiratory rate	Clinical, ventilator monitor
Respiratory distress	Use of accessory muscles, abdominal paradox
Mask comfort	Clinical
Compliance with ventilator setting	Clinical
Vital signs	Clinical
Physiology	
Arterial oxygen saturation	Pulse oximetry, arterial blood gas sample (frequently during first hours)
Arterial blood pressure	Clinical, monitoring (noninvasive)
ECG	
Ventilator setting	
Air leaks	Clinical, ventilator monitor
Patient–ventilator interaction	Clinical, ventilator monitor
Set parameters	Ventilator monitor

increase in delay time and in futile inspiratory efforts was observed [122]. When a resistive load was imposed, the inspiratory effort and patient–ventilator asynchrony increased and CO_2 clearance worsened [123, 124]. In one study, helmet and face mask were equally tolerated and both were effective in improving gas exchange and decreasing inspiratory effort [125]. The helmet, however, was less efficient in decreasing inspiratory effort and worsened the patient–ventilator interaction [125]. A recent report suggests the need for dedicated monitoring and alarming systems when using helmet CPAP to reduce the danger due to accidental failure of fresh gas source supply [126]. Regardless of the interface used, there is the need to reduce the risk of transmission of respiratory tract infections, such as careful fitting on the face, with potential risks for the caregivers. The addition of a viral-bacterial filter to the NPPV system between the mask and the exhalation port has been proposed [127].

Ventilatory setting

In theory, NPPV could be delivered with similar modalities as through an endotracheal or a tracheostomy cannula. In real life, the circumstances of ventilation and the equipment available are different [128]. Mask ventilation is now almost exclusively delivered by pressure-cycled ventilators (usually in pressure support or so-called bi-level ventilation), although no differences in success rate were found when NPPV was applied by means of volume-cycled ventilators [129]. In addition, PAV (a mode of partial ventilatory assistance endowed with characteristics of proportionality and adaptability to the intensity and timing of spontaneous ventilatory patterns) was used as an experimental modality of NPPV. Mask PAV was effective in improving arterial blood gases and reducing work of breathing in severe AECOPD [130], but it was not clinically superior to mask pressure support in multicentre studies [131, 132]. It seems that in real life this modality has no role in the routine NPPV treatment of ARF.

There is no definite guideline on optimal ventilator settings. The theoretical level of inspiratory and expiratory pressures to be applied in different diseases (*e.g.* peak inspiratory pressure support to increase tidal volume and PEEP to compensate for threshold load imposed by intrinsic PEEP in COPD patients) may not be the same as that applied through an ETI or a mask. The decision must take into consideration the ability to reduce work of breathing by providing an adequate level of pressure support against the discomfort and greater air leakage imposed by higher pressures. In fact, the patient's compliance with the ventilatory setting is the key factor influencing the choice of parameters [133].

Leaks and ventilators: ICU versus home

The presence of gas leaks is a near-constant feature of NPPV and may affect triggering of the ventilator, delivered F_{I,O_2} and air humidification. Differences can be found depending on the ventilator used (home *versus* ICU ventilators). In this regard, the importance of the inspiratory flow rate setting to reduce the leaks must be stressed [134]. While home ventilators can adequately compensate large gas leaks, ICU ventilators are not able to cope with large leaks and need to titrate trigger sensitivity to avoid auto-triggering and asynchrony between patient and ventilator [135–137]. Indeed, the presence of asynchrony represents one of the main problems with NPPV both during ARF episodes [138] and in long-term ventilation for chronic respiratory insufficiency [139]. In this regard, the recording of breathing frequency using the ventilator monitor may be misleading. Conversely, home ventilators usually have no facility to monitor the delivered F_{I,O_2}, which is crucial during hypoxaemic ARF. The results of a bench-model study [140] confirm that leaks interfere with several key functions of ICU ventilators. Overall, NPPV modes can correct part or all of this interference, but with wide variations between machines in terms of efficiency. Clinicians should be aware of these differences when applying NPPV with an ICU ventilator. Ventilators designed for NPPV should be used. The use of

conventional ventilators designed for invasive ventilation should be strongly discouraged, since failure rates are inappropriately high. In any case, as stated previously, ventilators with the availability of monitoring of functions, such as airway pressures, tidal volume and airflow, are preferable.

Humidification

In normal subjects, heated humidification during nasal NPPV attenuates the adverse effects of mouth leak on effective tidal volume and nasal resistance, and improves overall comfort. Heated humidification should be considered as part of an approach to patients who are troubled with nasal symptoms, once the leak has been minimised [141]. Two humidifying devices are used with ICU ventilators: 1) heated humidifiers (HH); and 2) heat-moisture exchangers (HME). A physiological study suggests that, compared with HH, HME greatly increases work of breathing during NPPV in hypercapnic ARF [128]. Indeed, it has been shown that during NPPV, the increased dead space of an HME can negatively affect ventilatory function and gas exchange and decrease efficiency of NPPV in patients with ARF [142]. During helmet ventilation, humidification may be difficult, if not impossible.

COST-EFFECTIVENESS

According to the studies previously conducted in the ICU, NPPV may reduce the risk of intubation from 63 to 21% and the mortality rate from 25 to 9% in AECOPD; the numbers needed to treat (NNT) were 2.4 to prevent one ETI and 6.3 to prevent one death. Application of NPPV in the ward was found to reduce the probability of meeting criteria for ETI from 27 to 15%, and the real ETI rate from 11 to 6%; the NNT was 8.3 to prevent criteria for ETI and 20 to prevent real ETI [143]. NPPV has been shown to be cost effective in the ICU, resulting in an improved clinical outcome and reduced costs [144]. NPPV use in the ward also reduces mortality, the demand for intensive care and lowers the overall cost of treatment [145]. Studies specifically addressing the workload for the personnel working with NPPV found that the first 6–8 h are usually associated with a high level of workload, reflecting the need for the personnel to remain at the bedside until the patient has adapted to the ventilation [6, 18]. The implications of NPPV regarding financial and human resources compared with CMV are still unclear. There is evidence that some COPD patients with less severe ARF without failure of any other organ may be successfully treated with lower costs in the RIICU and even in the ward than in the ICU (fig. 2) [146].

WHAT'S NEW?

Helium–oxygen mixture

The use of a helium–oxygen mixture (heliox) during NPPV in AECOPD seems very promising in further reducing dyspnoea and work of breathing, as well as hospital length of stay, but not in improving the success rate [147–150]. The use of heliox is difficult due to the lack of availability of an approved heliox-delivery system, and appropriately designed RCTs are needed to define the role for heliox combined with NPPV in COPD patients [151].

Sedation

Despite the advantages of NPPV, in ARF a large number of failures are due to patient refusal to continue the often uncomfortable sessions. Therefore, sedation might have a role in the success of this procedure. A cross-sectional web-based survey [152] showed that most physicians infrequently use sedation and analgesic therapy for NPPV to treat ARF, but practices vary widely within and between specialties and geographic regions. A recent pilot study [153] shows that remifentanil-based sedation is safe and effective in the treatment of NPPV failure due to low tolerance.

CONCLUSIONS

Noninvasive positive pressure ventilation has assumed an important role in managing patients with acute respiratory failure. Even in conditions in which noninvasive positive pressure ventilation has strong evidence of success, patients should be monitored closely for signs of treatment failure and should be promptly intubated before a crisis develops. The application of noninvasive positive pressure ventilation by a trained and experienced team, with careful patient selection and choice of appropriate location and setting, should optimise patient outcomes. It should be made clear that noninvasive positive pressure ventilation is not a panacea nor the ''poor man's'' technique of mechanical ventilation. Conversely, it cannot replace endotracheal intubation in all circumstances.

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