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Mechanical ventilation: invasive *versus* noninvasive

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ABSTRACT: Mechanical ventilation is the most widely used supportive technique in intensive care units. Several forms of external support for respiration have long been described to assist the failing ventilatory pump, and access to lower airways through tracheostomy or endotracheal tubes had constituted a major advance in the management of patients with respiratory distress. More recently, however, new "noninvasive" ventilation (NIV) techniques, using patient/ventilator interfaces in the form of facial masks, have been designed.

The reasons for promoting NIV include a better understanding of the role of ventilatory pump failure in the indications for mechanical ventilation, the development of ventilatory modalities able to work in synchrony with the patient, and the extensive recognition of complications associated with endotracheal intubation and standard mechanical ventilation.

NIV has been used primarily for patients with acute hypercapnic ventilatory failure, and especially for acute exacerbation of chronic obstructive pulmonary disease. In this population, the use of NIV is associated with a marked reduction in the need for endotracheal intubation, a decrease in complication rate, a reduced duration of hospital stay and a substantial reduction in hospital mortality. Similar benefits have also been demonstrated in patients with asphyxic forms of acute cardiogenic pulmonary oedema. In patients with primarily hypoxemic forms of respiratory failure, the level of success of NIV is more variable, but major benefits have also been demonstrated in selected populations with no contraindications such as multiple organ failure, loss of consciousness or haemodynamic instability.

One important factor in success seems to be the early delivery of noninvasive ventilation during the course of respiratory failure. Noninvasive ventilation allows many of the complications associated with mechanical ventilation to be avoided, especially the occurrence of nosocomial infections. The current use of noninvasive ventilation is growing up, and is becoming a major therapeutic tool in the intensive care unit.

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Without mechanical support for respiration, many patients would die within hours to days due to acute hypoxaemic and hypercapnic respiratory failure. Observational, physiological and case/control studies form a large body of evidence demonstrating that noninvasive ventilation (NIV) can be used in many situations to decrease a patient's dyspnoea and work of breathing, improve gas exchange and ultimately avoid the need for endotracheal intubation (ETI) [1–3]. Randomised controlled trials have confirmed this and helped delineate when NIV should be used as a first-line treatment. Studies conducted outside the context of clinical trials are also of great importance in ensuring that the results of these trials can be obtained in real life [4–6]. Indeed, the success of NIV may follow a learning curve, and early results may not be as good as those obtained later. In addition, it must be clear to clinicians that NIV is a complementary technique and cannot replace ETI in all instances.

In theory, the modes and settings for the delivery of NIV could be very similar to those for traditional mechanical ventilation through an endotracheal tube or tracheotomy cannula. In practice, because the circumstances of ventilation are different, the population of patients more selected and the equipment available sometimes more limited, this is not the case. In addition, leaks are a quasiconstant feature of NIV [7, 8]. NIV is usually delivered in the form of assisted ventilation, in which every breath is supported by the ventilator. Rarely, controlled mechanical ventilation is used.

Acute exacerbation of chronic respiratory failure

Patients with hypercapnic forms of acute respiratory failure are most likely to benefit from NIV [1–3]. Their respiratory muscles become unable to generate adequate alveolar ventilation despite large pressure swings because of the presence of severe abnormalities in respiratory mechanics (intrinsic positive end-expiratory pressure (PEEP) and high inspiratory resistances) [9]. Stimulation of the respiratory centres and the large negative intrathoracic pressure swings generated do not permit compensation for these abnormalities; rapid shallow breathing ensues, associated with carbon dioxide retention and respiratory acidosis, and a risk of respiratory muscle fatigue. Dyspnoea, right ventricular failure and encephalopathy characterise the severe acute exacerbation. Delivery of NIV allows the patient to take deeper breaths with less effort. NIV at two levels of pressure (pressure support [10] and PEEP [11]) delivers a positive inspiratory pressure swing in synchrony with the patient's inspiratory effort. A low level of pressure during expiration counterbalances the effects of dynamic hyperinflation, which

result in a positive residual alveolar pressure at the end of expiration. The combination of the two levels of pressure has the greatest efficacy in reducing patient effort [12]. NIV can reverse the clinical abnormalities related to hypoxaemia, hypercapnia and acidosis [9, 13].

Clinical trials

The efficacy of NIV in the case of acute exacerbation of chronic obstructive pulmonary disease (COPD) has been extensively studied (table 1). A recent international consensus conference recommended that NIV be considered a first-line treatment in these patients [24], and British Thoracic Society guidelines recommend that every hospital should be able to deliver NIV on a round-the-clock basis in this indication [25]. In 1990, a case/control study first demonstrated that NIV could markedly reduce the need for ETI [9]. Subsequently, several prospective randomised trials confirmed that NIV reduces the need for ETI and the rate of complications, shortens the duration of hospital stay and improves survival in patients with COPD [14–16, 18–20, 26]. In a prospective randomised trial, KRAMER *et al.* [15] found a major reduction in the need for ETI. In this study, 74% of patients had COPD and the reduction in ETI rate in this group was from 67 to 9%. Two studies, conducted in the UK, demonstrated the efficacy of NIV outside the intensive care unit (ICU) [14, 20]. In the largest study in the ICU, in which 85 patients with COPD were randomised to treatment with or without face mask pressure support ventilation [16], the ETI rate was 74% for controls receiving standard medical treatment compared to only 26% in the NIV group. This reduction was associated with fewer complications during the ICU stay, a reduced duration of hospital stay and, more importantly, a significant reduction in mortality rate (from 29 to 9%). The overall decrease in mortality was ascribable to reductions in the need for ETI and various ICU-related complications.

Two open studies also described the beneficial short-term effects of using NIV in asthmatic patients deteriorating despite medical therapy [27, 28].

Where to perform noninvasive ventilation

An early randomised trial in 60 patients performed by BOTT *et al.* [14] found major benefits of NIV performed in the emergency department or ward on dyspnoea and outcome, especially when the four patients who did not tolerate NIV were excluded from the analysis. A more recent prospective multicentric randomised trial conducted in the UK by PLANT *et al.* [20] compared standard therapy alone (control group) and with NIV in 236 COPD patients admitted to general respiratory wards due to acute respiratory failure. The failure (reaching criteria for ETI) rate was higher in the control group (27 *versus* 15%), and NIV was associated with a lower in-hospital mortality rate. Two specific aspects of this study need to be emphasised in order to explain the results. Owing to admission policy in the UK, all patients who failed NIV were not transferred to an ICU, and, for this reason, the results may not be extrapolated to all kinds of medical institution because the control group might have benefited from a more intensive approach in other institutions. The authors stressed the fact that, for the most severe patients (arterial blood pH of <7.30 on admission), the benefit of delivering NIV outside the ICU became marginal, with a high mortality rate. These patients would probably have benefited from early ICU admission for NIV delivery. The other aspect is the specific teaching and training of personnel before and during the course of the study. A strict protocol was followed during the study, with no individual titration. Very probably, this is a key element in explaining the benefits observed in the study. Other studies performed in emergency departments did not show similar benefits [17, 29], and, in one study, the results even suggested that ETI could have been delayed by inappropriate or inadequate use of NIV [29].

Table 1. – Randomised controlled clinical trials assessing the efficacy of noninvasive ventilation (NIV) in patients with chronic obstructive pulmonary disease (COPD)

First author [Ref.]	Patients n	Location/study	Impact of NIV
BOTT [14]	60	Ward	Improvement in ABGs, dyspnoea Reduction in ETI criteria Reduction in mortality (excluding 4 patients not on NIV)
KRAMER [15]	31 (74% COPD)	ICU	Improvement in ABGs, dyspnoea Reduction in ETI (67 to 9% in COPD)
BROCHARD [16]	84	ICU	Improvement in ABGs Reduction in ETI (74 to 26%), complications, LOS Reduction in mortality
BARBÉ [17]	24	Emergency ward	No benefit; no ETI required
ANGUS [18]	17	NIV *versus* doxapram	Improvement in ABGs
CELIKEL [19]	30	–	Improvement in ABGs Reduction in criteria for ETI, LOS
PLANT [20]	236	Ward	Improvement in ABGs Reduction in criteria for ETI Reduction in mortality
CONTI [21]	49	Late ICU admission and NIV	Reduction in ETI (48 to 100%) Similar ICU outcome Fewer long-term readmissions (65 *versus* 100%)
NAVA [22]	50	MV curtailment after 48 h	Improvement in weaning success Reduction of LOS, complications Reduction in mortality
GIRAULT [23]	33	MV curtailment after 4–5 days	Shorter duration of ETI No change in outcome Longer duration of ventilation

ABGs: arterial blood gases; ETI: endotracheal intubation; ICU: intensive care unit; LOS: length of stay; MV: mechanical ventilation.

Workload for the personnel

In the study of PLANT *et al.* [20], the training period comprised 8 h over the 3 months preceding the study and 1 h monthly during the trial. Three studies specifically studied the workload for the personnel associated with the use of NIV. They found a different distribution of workload compared to a more traditional approach towards patients with respiratory failure [15, 20, 30]. The first 6–8 h of NIV are usually associated with a high level of workload, reflecting the need for personnel to remain at the bedside.

When to perform noninvasive ventilation

Early NIV to prevent further deterioration must become an important part of the first-line therapy of acute exacerbation of COPD [31]. A very low arterial blood pH, marked alteration in mental status when NIV is started, and the presence of comorbid conditions or a high severity score characterise patients who experience NIV failure [1, 32]. The presence of several of these factors seems to indicate that late delivery of NIV during the course of the exacerbation reduces the likelihood of success. Every effort should be made to deliver NIV early, and close monitoring is therefore in order when NIV is started late. In addition, a recent randomised controlled trial indicates that the efficacy of NIV diminishes when this therapy is applied late in the course of the exacerbation. Indeed, CONTI *et al.* [21] studied patients at a very late stage, and showed a reduction in ETI from 100 to 52%, which was associated with only marginal short-term benefits. NIV was applied to patients with COPD who had stayed a mean of 14 h in the emergency ward before being admitted to the ICU, when, before the advent of NIV, ETI and mechanical ventilation would have been the usual treatment. Interestingly, there were still significant long-term benefits associated with the use of NIV, such as a decrease in the readmission rate and the need for long-term oxygen therapy.

Long-term survival

Three studies have suggested that the use of NIV is associated with a better 1-yr survival compared to standard ICU therapy [33, 34] or invasive mechanical ventilation [35]. The recent study of CONTI *et al.* [21] confirms these findings.

Negative pressure ventilation

Nowadays, the technique of negative pressure ventilation is only available in very few centres in the world. It should be mentioned, however, that negative pressure ventilation was the first mode of delivering noninvasive ventilation, before positive pressure ventilation became the rule in the 1950s [36, 37]. Its efficacy in the treatment of acute exacerbations of COPD may be superior, in experienced hands, to a traditional approach with invasive mechanical ventilation, and similar to noninvasive ventilation *via* a face mask [38, 39].

Helium-oxygen mixture

The use of a helium/oxygen mixture during NIV seems very promising for further reducing dyspnoea and work of breathing in patients with COPD [40, 41]. Several randomised controlled trials are in progress to test the hypothesis that this gas mixture could increase the success rate of this technique.

Cardiogenic pulmonary oedema

Pathophysiology

Continuous positive airway pressure (CPAP) has the ability, by raising intrathoracic pressure, to decrease shunting and improve arterial oxygenation and dyspnoea in patients with acute cardiogenic pulmonary oedema [42–47]. CPAP can both lessen the work of breathing substantially and improve cardiovascular function by decreasing the left ventricular afterload in nonpreload-dependent patients [46]. Pressure support plus PEEP induces similar pathophysiological benefits.

Most patients with cardiogenic pulmonary oedema improve rapidly with medical therapy. A few, however, develop acute asphyxic respiratory distress and require ventilatory support until the medical treatment starts to work. This may be particularly common in elderly patients with heart disease and patients with concomitant chronic lung disease [48]. Several NIV modalities have been tried successfully, the goal being to avoid ETI.

Continuous positive airway pressure or pressure support plus positive end-expiratory pressure

Randomised trials comparing either CPAP or pressure support plus PEEP to standard medical therapy found similar results with the two techniques in terms of improvement in arterial blood gas levels and respiratory frequency. Both CPAP and pressure support plus PEEP significantly reduced the ETI rate [43, 44, 47, 49, 50]. Two studies, however, indicate a need for caution. One compared pressure support plus PEEP and CPAP [51]. Acute myocardial infarction was more common in the pressure support group than in the CPAP group and it remains unclear whether this should be ascribed to a randomisation bias or to a deleterious effect of pressure support plus PEEP itself. A high rate of acute myocardial infarction was not found in the NIV arm of a randomised controlled trial with pressure support and PEEP, nor in observational studies [47, 49, 50]. The second study compared intravenous bolus therapy with high-dose nitrates to conventional medical therapy (a different medical therapy) and pressure support plus PEEP. The first of these two treatments was far more clinically effective than NIV and resulted in a better outcome [52]. These two studies draw attention to the vulnerability of patients with cardiogenic pulmonary oedema, particularly those with ischaemic heart disease. They indicate that both appropriate drug therapy and close monitoring are in order when using any form of NIV, especially in patients with ischaemic heart disease.

Hypoxaemic respiratory failure

Positive pressure ventilation was reintroduced during the first half of the twentieth century, for support of patients requiring general anaesthesia for surgery, especially thoracic procedures. When the earliest case series of patients with adult respiratory distress syndrome were reported in the late 1960s [53], positive pressure ventilation was used with increasing frequency for nonsurgical patients with acute respiratory failure of various causes, including obstructive airways disease and severe pneumonia. NIV was proposed, in the early 1990s, for treating these patients, but initial studies have not all been successful [27, 54, 55]. More recently, new trials with careful selection of patients have demonstrated clear benefits of NIV [56–58].

Continuous positive airway pressure

A recent investigation evaluated whether CPAP *via* a face mask produced physiological benefits and reduced the need for ETI in patients with acute lung injury [59]. CPAP was associated with an early favourable physiological response in terms of comfort and oxygenation during the first hour. However, no differences were found in the need for ETI, in-hospital mortality or duration of ICU stay. In addition, use of CPAP was associated with more complications, including stress ulcer bleeding and cardiac arrest at the time of ETI. These results suggest that CPAP alone cannot be recommended for avoiding ETI in patients with acute lung injury. Its use should be limited to a short initial period if no other method is available.

Pressure support and positive end-expiratory pressure

Until the late 1990s, the most convincing successes with NIV were obtained in patients with acute respiratory acidosis in whom hypoxaemia was not the main reason for respiratory failure. One randomised controlled trial, of WYSOCKI *et al.* [55], found no benefit of NIV in patients with no previous history of chronic lung disease, except in the subgroup of patients who developed acute hypercapnia. However, the beneficial effects of NIV have now been extended to different forms of hypoxaemic respiratory failure with carefully selected patients, showing that NIV may reduce the need for ETI and improve outcomes [26, 56–58, 60, 61]. ANTONELLI *et al.* [56] showed marked benefits of NIV using pressure support and PEEP in hypoxaemic patients free from COPD, haemodynamic instability or neurological impairment, who were randomised when they reached predefined criteria for ETI. Improvements in oxygenation were similar with both the noninvasive and the invasive approach. Despite a 30% failure rate, patients treated with NIV showed a shorter duration of ventilation and ICU stay and experienced fewer complications. Thus NIV can be effective in selected patients with hypoxaemic respiratory failure but with no haemodynamic or mental impairment.

Immunosuppressed patients

One of the main benefits of NIV may be a reduction in the risk of infectious complications [5, 6]. Therefore, patients at high risk of nosocomial infection when mechanically ventilated may be particularly likely to benefit from NIV. Several recent trials have shown major benefits of NIV as a preventive measure during episodes of acute hypoxaemic respiratory failure in solid organ transplant patients or patients with severe immunosuppression, particularly related to haematological malignancies and neutropenia [57, 60, 62]. The rates of ETI and infectious complication, duration of stay, and mortality were significantly reduced by use of NIV. Early initiation of NIV seems necessary to avoid ETI and provide benefit to patients.

Patients suffering from *Pneumocystis carinii* pneumonia during the course of human immunodeficiency virus infection may also benefit from NIV, as shown in the case/control study of CONFALONIERI *et al.* [63]

Lung surgery

Several studies looked at the use of NIV after lung surgery [64–66]. AURIANT *et al.* [64] conducted a randomised controlled trial in patients who experienced respiratory distress after lung resection. The reason why ETI should be avoided is the very poor outcome of patients, who usually require reintubation shortly after lung surgery. A reduction in ETI rate and a clear benefit in terms of hospital survival was observed with NIV. A noncontrolled study suggested interesting results using NIV after bilateral lung transplantation [65].

Community-acquired pneumonia

CONFALONIERI *et al.* [26], in a randomised controlled trial, showed major benefit of NIV in patients with community-acquired pneumonia, by reducing the rate of ETI and complications and duration of stay. This benefit, however, was almost entirely explained by the subgroup of patients with COPD. Other studies with severely hypoxaemic patients with pneumonia have shown a high rate of failure in this subgroup [27, 32, 67]. NIV cannot be recommended for all patients with severe community-acquired pneumonia.

Noninvasive ventilation in the postextubation period

The physiological rationale for this approach was recently demonstrated by VITACCA *et al.* [68]. HILBERT *et al.* [69] suggested favourable effects of NIV on preventing reintubation in patients with COPD in a case/control study. A recent prospective randomised trial by KEENAN *et al.* [70] was performed in all patients experiencing postextubation respiratory distress. This study did not show any benefit of NIV. Two other prospective randomised trials did not find any preventive effect of NIV [71, 72]. The benefits of this technique may thus be observed only in patients with COPD, and the efficacy of NIV in preventing reintubation in all patients remains unproven.

A number of patients with COPD still require ETI because they fail NIV, show a contraindication to NIV (such as a need for surgery) or exhibit criteria requiring immediate ETI. However, when there is a need for prolonged ventilatory assistance, these patients may be switched to NIV after a few days of ETI, as a means of deliberately reducing the duration of invasive ventilation [22, 23]. This approach was shown, in two randomised controlled trials, to reduce the duration of ETI [22, 23]. In one study only, complications were reduced and survival rate was higher at day 60 with this approach [22]. Lastly, NIV can also be proposed in persistent weaning failure. FERRER *et al.* [73] recently reported the results of a prospective randomised controlled trial in 43 mechanically ventilated patients who had failed a weaning trial for 3 consecutive days and were randomly extubated, receiving NIV, or remained intubated following a conventional weaning approach. Earlier extubation with NIV resulted in a shorter duration of mechanical ventilation and stay, less need for tracheotomy, a lower incidence of complications and improved survival in these patients.

Patients not to be intubated

Several reports have described the effects of NIV in patients with acute respiratory failure who were poor candidates for ETI because of advanced age, debilitation or a "do not resuscitate" order [74, 75]. The overall success rate in these reports was ~60–70%. Gas exchange improved rapidly in successfully treated patients. Even when respiratory failure

did not resolve, NIV provided symptomatic relief from dyspnoea.

Noninvasive ventilation during fibreoptic bronchoscopy

Several studies have suggested or demonstrated that fibreoptic bronchoscopy could be performed during delivery of NIV (CPAP for hypoxaemic patients or pressure support plus PEEP), and that this approach improved tolerance of bronchoscopy and could prevent subsequent complications and the need for ETI [76, 77].

Conclusion

The success of noninvasive ventilation is dependent on various clinical aspects and the organisation of care, but also on a lot of technical issues. Far from being details, they can make a large difference [1, 78]. They include the patient/ventilator interface [79–81], type of humidifier [8] and ventilator used and its capabilities for triggering and pressurisation [30, 82, 83]. The general care of the patient is different from that for a patient receiving invasive ventilation, and will thus potentially greatly influence the success of the technique. There is now a good evidence base for the use of noninvasive ventilation in numerous different conditions and settings; however, it remains a complementary therapy to invasive ventilation and clinicians need to be aware of the contraindications.

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