Noninvasive Ventilation for Chronic Obstructive Pulmonary Disease

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Summary

Noninvasive positive-pressure ventilation (NPPV) should be considered a standard of care to treat COPD exacerbations in selected patients, because NPPV markedly reduces the need for intubation and improves outcomes, including lowering complication and mortality rates and shortening hospital stay. Weaker evidence indicates that NPPV is beneficial for COPD patients suffering respiratory failure precipitated by superimposed pneumonia or postoperative complications, to allow earlier extubation, to avoid re-intubation in patients who fail extubation, or to assist do-not-intubate patients. NPPV patient-selection guidelines help to identify patients who need ventilatory assistance and exclude patients who are too ill to safely use NPPV. Predictors of success with NPPV for COPD exacerbations have been identified and include patient cooperativeness, ability to protect the airway, acuteness of illness not too severe, and a good initial response (within first 1–2 h of NPPV). In applying NPPV, the clinician must pay attention to patient comfort, mask fit and air leak, patient-ventilator synchrony, sternocleidomastoid muscle activity, vital signs, hours of NPPV use, problems with patient adaptation to NPPV (eg, nasal congestion, dryness, gastric insufflation, conjunctival irritation, inability to sleep), symptoms (eg, dyspnea, fatigue, morning headache, hypersomnia), and gas exchange while awake and asleep. For severe stable COPD, preliminary evidence suggests that NPPV might improve daytime and nocturnal gas exchange, increase sleep duration, improve quality of life, and possibly reduce the need for hospitalization, but further study is needed. There is consensus, but without strong supportive evidence, that COPD patients who have substantial daytime hypercapnia and superimposed nocturnal hypoventilation are the most likely to benefit from NPPV. Adherence to NPPV is problematic among patients with severe stable COPD. Key words: chronic obstructive pulmonary disease, COPD, noninvasive ventilation, mechanical ventilation, acute respiratory failure. [Respir Care 2004;49(1):72–87. © 2004 Daedalus Enterprises]
Introduction

Noninvasive positive-pressure ventilation (NPPV), the provision of ventilatory assistance without airway invasion, has seen increasing use in critical care units, to avoid endotracheal intubation and its attendant complications.\(^1\)\(^2\) Treatment of acute respiratory failure (ARF) caused by COPD exacerbation is the best-studied acute application of NPPV and is coming to be viewed as a standard of care. In contrast, NPPV for severe stable COPD has been controversial because of conflicting evidence and problems with application. This report will examine the evidence supporting the use of NPPV for various applications in COPD and make recommendations on patient selection as well as technical aspects of NPPV application in COPD.

[Fig. 1. Schema comparing chest wall configuration at functional residual capacity of a normal individual (left hemithorax) and a patient with chronic obstructive pulmonary disease (COPD, advanced emphysema) (right hemithorax). The COPD patient has a flattened diaphragm, which increases the radius of curvature and increases the tension (and, hence, impedance to blood flow) for a given pressure. The COPD patient’s ribs are horizontal and the zone of apposition between the pleural surfaces is reduced, greatly reducing the diaphragm’s efficiency in expanding the chest wall. The use of accessory muscles to assist inspiration at high lung volumes augments the oxygen cost of breathing. Also, intrinsic positive end-expiratory pressure (auto-PEEP) poses an additional work load, requiring that the inspiratory muscles lower alveolar pressure to a subatmospheric level to initiate airflow for the next breath.

During a COPD exacerbation, a precarious situation becomes potentially catastrophic. Related to increased airway resistance, lung elastance, hypoxemia, or some combination of these factors, the demand for breathing work increases while the capacity to supply the work becomes further compromised. Although exacerbations are often accompanied by worsening alveolar hypoventilation, the drive to breathe is increased and muscle fatigue (characterized by reduced muscular performance despite steady or increased neural drive) may develop. Often, in a futile attempt to compensate, lungs become more hyperinflated, relying even more on accessory muscles. Respiratory rate increases in response to the increased drive, shortening the expiratory time and exacerbating auto-PEEP. This further increases the inspiratory load, adding to the imbalance of supply and demand for breathing work. A vicious cycle ensues, leading to respiratory muscle fatigue, ventilatory failure, and death, unless therapeutic interventions interrupt the cycle. Traditionally, these have included efforts to

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reduce airway resistance with bronchodilators, anti-inflammatory agents, cautious oxygen supplementation, and antibiotics. In the past, if these measures failed, clinicians would resort to assisted ventilation, usually via endotracheal intubation, unless the patient declined, in which case comfort measures would be offered.

The traditional approach was often effective, with survival rates to hospital discharge averaging 70% for COPD patients treated with invasive mechanical ventilation for respiratory failure. However, complications of invasive mechanical ventilation, including upper airway trauma, pneumothorax, and nosocomial infection occurred and added to morbidity and mortality. NPPV has appeal for treating COPD exacerbations because it is an effective way of providing partial ventilatory assistance while avoiding many of the complications of invasive mechanical ventilation. When it combines applied PEEP to counterbalance auto-PEEP, and pressure support to assist inspiration, NPPV reduces transdiaphragmatic pressure more than either applied PEEP or pressure-support alone. Thereby, it has the potential to serve as a “crutch” while medical therapies are given time to ameliorate the underlying physiologic defects, and intubation can be avoided.

**Acute Applications of NPPV with COPD Patients**

**COPD Exacerbations**

Using historically-matched controls, Brochard et al were the first to show that pressure-support ventilation administered via face mask significantly reduced the need for intubation, duration of mechanical ventilation, and intensive care unit (ICU) stay in patients with COPD exacerbations. Subsequently, a number of randomized, controlled trials confirmed those findings. Bott et al reported significantly greater improvements in $P_{aCo_2}$ and dyspnea scores within the first hour in a group of NPPV-treated patients than in randomized control subjects. Also there was a 10% mortality rate in the NPPV group, compared to 30% among controls, though that difference was not statistically significant unless the analysis excluded the 4 patients who were randomized to receive NPPV but did not receive it.

Kramer et al subsequently found that NPPV reduced the rate of endotracheal intubation to 9% from 67% among controls in a subgroup of COPD patients. That study also showed more rapid improvement in respiratory rate and blood gas values in the NPPV group but no significant differences in hospital stay or mortality rate, though that lack of significant difference might have been due to small sample size.

In a multicenter European trial with 85 patients, Brochard et al found that vital signs, blood gas values, and encephalopathy scores improved more rapidly in the NPPV group than in controls, and intubation rates (74% vs 26%), complication rates (notably pneumonia and other complications from endotracheal intubation), hospital stay (35 d vs 17 d), and mortality rate (31% vs 9%) were significantly better among the NPPV group. In a smaller trial by Celik et al, NPPV significantly reduced intubation rate and hospital stay, from 14.6 d to 11.7 d ($p < 0.05$), compared to controls.

In a study using NPPV not just at academic medical centers (thus providing information more relevant to “real world” applications), Plant et al randomized 236 patients suffering COPD exacerbations to receive either NPPV or standard therapy, administered by nurses in general medical respiratory wards. Intubation and mortality rates were significantly lower in the NPPV group than in the control group (15% vs 27%, $p = 0.02$, and 10% vs 20%, $p = 0.05$, respectively), and the study confirmed the earlier findings of more rapid improvements in arterial pH, respiratory rate, and breathlessness in the NPPV group. Notably, the mortality benefit was not apparent in patients with pH < 7.30, and the authors surmised that this more severely ill subgroup would have fared better in a more closely monitored setting such as an ICU.

In the only study with negative findings, Barbe et al observed that NPPV failed to lower intubation or mortality rate or hospital stay in consecutive patients admitted to the hospital with COPD exacerbations, but it is notable that no intubations or mortalities occurred in the control group. Furthermore, duration of hospital stay was only one third that of the control group in the Brochard study and the baseline blood gas values were not as severely altered as in most of the other controlled trials. The study’s most important finding was that patients with relatively mild COPD exacerbations are not likely to benefit from NPPV, which suggests that NPPV should be applied to selected patients who have a demonstrable need for ventilatory assistance.

Taken together, the above studies demonstrate that NPPV is effective for moderate-to-severe COPD exacerbations, not only to effect rapid symptomatic and physiologic improvement but also to significantly reduce the intubation, complication, and mortality rates, and (some studies suggest) hospital stay. Several meta-analyses combining the results of those studies reached similar conclusions about the intubation and mortality rates. In their meta-analysis Keenan et al found that NPPV was effective at treating COPD exacerbations and reducing the cost of hospitalization by approximately $3,200 (in 1996 Canadian dollars), compared to standard therapy. More recently, Peter et al analyzed the results of studies of NPPV effectiveness for ARF in general and found the greatest benefit in the COPD subgroup. Most recently meta-analyses by Lightowler et al (in a Cochrane systematic review) and Keenan et al reported similar findings regarding the use of NPPV for COPD exacerbations. Both found signif-
icantly lower mortality rate (relative risk 0.41, risk reduction 10%) and less need for intubation (relative risk 0.42, risk reduction 28%). In addition, both found shorter durations of hospitalization (−3.24 d and −4.57 d, respectively) and Lightowler et al found significantly greater improvements in $P_aCO_2$ and respiratory rate after 1 hour in NPPV-treated patients than in controls. Further, Keenan et al found that these benefits were demonstrable in severe but not in mild exacerbations. Based on that evidence, the authors of the meta-analyses and the participants in the consensus groups opined that NPPV should be used early in the course of a COPD exacerbation. I have argued elsewhere that NPPV should now be considered a standard of care for moderate-to-severe COPD exacerbations.

NPPV for COPD Patients in Special Circumstances

NPPV for COPD Complicated by Pneumonia. The presence of pneumonia has been associated with poor outcome in patients treated with NPPV. However, in one randomized trial with patients suffering “severe community-acquired pneumonia,” defined as severe hypoxemia (ratio of $P_aO_2$ to fraction of inspired oxygen $[P_aO_2/F_I O_2] < 200$ mm Hg) and respiratory distress (respiratory rate $> 35$ breaths/min), NPPV reduced the need for intubation (21% vs 50%, $p = 0.03$), shortened ICU stay (1.8 d vs 6 d, $p = 0.04$), and reduced mortality among the COPD subgroup of patients 2 months after hospital discharge (11% vs 63%). Moreover, a post hoc analysis revealed that the COPD subgroup was the only one to benefit from NPPV. Thus, the study indicates that even when complicated by community-acquired pneumonia, COPD exacerbation is an appropriate indication for NPPV. It leaves unanswered whether NPPV should be used for severe community-acquired pneumonia in non-COPD patients.

NPPV for Postoperative Patients. Early case series reported successful use of NPPV to treat respiratory insufficiency after surgery in patients with $P_aCO_2 > 50$ mm Hg, $P_aO_2 < 60$ mm Hg, or evidence of respiratory muscle fatigue. More recently a randomized trial of NPPV in post-lung-resection patients with acute respiratory insufficiency showed significantly less need for intubation, shorter ICU stay, and lower mortality rate than conventionally-treated controls. Although only a portion of those patients had COPD, accumulating evidence now supports the use of NPPV in selected postoperative patients (including COPD patients) to maintain improved gas exchange and avoid reintubation and its attendant complications. However, NPPV should not be used in patients who have had recent neck, upper airway, or esophageal surgery.

NPPV to Facilitate Early Exubation. NPPV has been used to facilitate early extubation after bouts of ARF and to avoid extubation failure when patients deteriorate after extubation. In the former instance NPPV is used to expedite extubation in patients who fail to meet standard extubation criteria. The rationale is that outcomes can be improved by shortening the duration of invasive mechanical ventilation in patients who become good candidates for NPPV (ie, able to cooperate, capable of airway protection, otherwise medically stable) but fail standard extubation criteria. Early removal of the endotracheal tube is hypothesized to reduce the complications of prolonged intubation (ie, nosocomial infection and upper airway trauma). The first controlled trial to test this idea randomized 50 COPD patients who had been intubated for 48 hours and who failed a T-piece spontaneous-breathing trial. The patients were randomized to either the standard weaning procedure or to extubation and NPPV. Compared to the controls, the extubation/NPPV group had a higher overall weaning rate after 60 days (88% vs 68%), a shorter duration of mechanical ventilation (10.2 d vs 16.6 d), brief ICU stay (15.1 d vs 24 d), and better 60-day survival (92% vs 72%) (all $p < 0.05$). In addition, NPPV-treated patients had no nosocomial pneumonias, compared to 7 in the control group.

A subsequent trial of 33 patients randomized to early extubation and NPPV or conventional intubation with standard weaning addressed the question of whether NPPV should be used as a “systematic” extubation technique. The extubation/NPPV group had a shorter duration of invasive mechanical ventilation than the control group (4.56 d vs 7.69 d, $p < 0.05$) but actually had a greater total duration of mechanical ventilation (including the time on NPPV) (16.1 d vs 7.69 d, $p = 0.0001$). Furthermore, patients in the NPPV group had similar eventual weaning and mortality rates, and although they had a tendency toward fewer complications (9% vs 16%), the difference was not statistically significant. The authors concluded that NPPV shortens the duration of invasive mechanical ventilation, but they were unable to demonstrate significant improvements in other outcomes.

Most recently, a randomized, controlled trial of NPPV to facilitate weaning in 43 patients with “persistent weaning failure” (failure of spontaneous breathing trials on 3 consecutive days) showed significantly shorter ICU and hospital stays, a lower incidence of nosocomial pneumonia (59% vs 24%, $p < 0.05$), better hospital and 90-day mortality (odds ratio 3.5), and fewer complications. Nineteen of the 43 patients had COPD exacerbations, and another nine had congestive heart failure, which predisposed the study to favorable results.

In summary, randomized, controlled trials of early extubation to NPPV with COPD patients have yielded mixed results, 2 studies showing significant benefit and the other showing no important benefit, but no attributable harm either. Intubated COPD patients are appropriate candidates...
for early extubation to NPPV, but clinicians are advised to use caution when selecting patients. The inability to sustain 5–10 min of unassisted breathing, a prior difficult intubation, multiple co-morbidities, copious secretions, a weakened cough, or the need for high levels of pressure support prior to extubation (> 20 cm H₂O) should exclude patients from consideration for early extubation.

NPPV to Prevent Extubation Failure. NPPV can be used to avoid reintubation in patients who fail extubation. Extubation failure occurs after 5–20% of planned and 40–50% of unplanned extubations and is associated with a mortality of 43%, compared to only 12% in those who succeed extubation. Several nonrandomized studies of patients with ARF of diverse etiologies support the idea that NPPV can obviate reintubation in certain patients who suffer extubation failure, thereby avoiding the complications and mortality of prolonged intubation. One study specifically of COPD patients found that NPPV lowered the reintubation rate (20% vs 67%, p < 0.05) and ICU stay in 30 patients, compared to 30 historical controls. In a subsequent randomized trial of patients at high risk for extubation failure and who developed respiratory distress within 48 hours of extubation, however, NPPV did not reduce the need for intubation, duration of mechanical ventilation, hospital stay, or mortality. However, COPD patients were excluded from that study after the first year because of ethical concerns. A more recent international randomized trial of over 200 patients at high risk for extubation failure randomized to NPPV or standard therapy showed an increased mortality in the NPPV group, most likely related to delayed intubation. That study has been reported thus far only in preliminary form, and just 13% of the patients had COPD.

In summary, the use of NPPV to avoid extubation failure is supported by a historically controlled study but no randomized, controlled trials. On the other hand, the likelihood is that if NPPV is effective in de novo COPD exacerbations leading to respiratory failure, it is also effective in the postextubation setting. Furthermore, many investigators have ethical concerns about subjecting COPD patients in this setting to a randomized trial, because of the need to randomly subject them to the risk of intubation, which might add to their morbidity or even mortality. Thus, the best current recommendation is to use NPPV for postextubation COPD patients with incipient respiratory failure, but to be careful to ascertain that they are good NPPV candidates, and to avoid delays in intubation in the face of deterioration.

NPPV for Do-Not-Intubate Patients. The use of NPPV to treat respiratory failure in patients who have declined intubation is common in some centers, accounting for some 10% of acute NPPV applications in a recent survey. Some have argued that there is little to lose with this approach, as it may reverse the acute deterioration or at least provide relief of dyspnea and a few extra hours to finalize affairs. Others have argued, on the other hand, that this merely prolongs the dying process, consumes resources inappropriately, and may add to discomfort or may be counter to patients’ wishes about life-prolonging measures. In a study of 30 patients, most with COPD, in whom endotracheal intubation was “contraindicated or postponed,” 18 patients (60%) were successfully supported with NPPV and weaned. Another uncontrolled series observed a similar response to NPPV among 26 patients with acute hypercapnic and hypoxemic respiratory failure who refused intubation. In a more recent prospective survey of 113 do-not-intubate patients treated with NPPV, survival to hospital discharge was 75% and 52% for acute pulmonary edema and COPD patients, respectively, whereas it was < 25% for those with diagnoses of pneumonia or cancer. Thus, NPPV is indicated in do-not-intubate patients with acutely reversible processes that are known to respond well, including COPD exacerbations. However, if NPPV is to be used with a do-not-intubate patient, the patient and/or the family should be informed that NPPV is being used as a form of life support that may be uncomfortable and can be removed at any time.

Patient Selection. Selection of appropriate patients is key to the successful application of NPPV. The selection process takes into consideration a number of factors, including the patient’s diagnosis, clinical characteristics, and

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<th>Table 1. Predictors of Success for NPPV in the Acute Setting</th>
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<td>Cooperative</td>
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<td>Able to Protect Airway</td>
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<td>Not Too Acutely Ill</td>
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<td>Good Initial Response to NPPV (within first 1–2 h)</td>
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NPPV = noninvasive positive-pressure ventilation
*Compliance refers to the clinician’s assessment of the patient’s acceptance of the technique
APACHE = acute physiology and chronic health evaluation
(Adapted from References 21 and 41)
risk of failure, and ultimately becomes a clinical judgment depending largely on physician experience.

Predictors of NPPV success have been identified (Table 1).\textsuperscript{21-41,42} Patients with a better neurologic status (and hence who are more cooperative), who can adequately protect the airway, and who have not developed severe acid-base or gas-exchange derangements are more likely to succeed. Several studies have also found that initial improvements in $\text{pH}$, $P_{\text{aCO}_2}$, and level of consciousness after 1 hour of NPPV are strong indicators of success.\textsuperscript{41,42} These studies indicate that there is a “window of opportunity” when initiating NPPV, which opens when the patient becomes distressed enough to warrant ventilatory assistance and closes if the patient progresses too far and becomes severely acidemic. Thus, early initiation of NPPV is recommended so that patients have time to adapt and respiratory crises can be averted. Contrariwise, NPPV begun too early might be unhelpful and wasteful of resources, because many treated patients might do well without any ventilatory assistance. For this reason selection guidelines recommend first establishing the need for ventilatory assistance according to clinical and blood-gas-value criteria (indicating that the window of opportunity has opened) and then excluding patients for whom NPPV is contraindicated or likely to fail (indicating that the window of opportunity has closed) (Table 2).

**Recommendations on NPPV for COPD Exacerbations**

Several consensus bodies have offered recommendations on the use of NPPV for COPD exacerbations. The

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<td>Moderate-to-severe respiratory distress</td>
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<tr>
<td>Tachypnea (respiratory rate $&gt;24$ breaths/min)</td>
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<td>Accessory muscle use or abdominal paradox</td>
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<td>Blood gas derangement: $\text{pH} &lt; 7.35$, $P_{\text{aCO}<em>2} &gt; 45$ mm Hg, or $P</em>{\text{aO}<em>2}/F</em>{\text{IO}_2} &lt; 200$ mm Hg</td>
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<th>Exclude Patients With Contraindications to NPPV</th>
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<tr>
<td>Respiratory arrest</td>
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<tr>
<td>Medically unstable (septic or cardiogenic shock, uncontrolled upper gastrointestinal bleeding, acute myocardial infarction with planned intervention, uncontrolled arrhythmia)</td>
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<tr>
<td>Unable to protect airway</td>
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<td>Excessive secretions</td>
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<td>Uncooperative or agitated</td>
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<tr>
<td>Unable to fit mask</td>
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<td>Recent upper-airway or upper-gastrointestinal surgery</td>
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NPPV = noninvasive positive-pressure ventilation
COPD = chronic obstructive pulmonary disease
$F_{\text{IO}_2}$ = fraction of inspired oxygen
(Adapted from Reference 43)

1997 *Respiratory Care* Journal Conference on NPPV concluded that evidence was accumulating to support the use of NPPV for COPD exacerbations in the acute care setting, but recommended further study.\textsuperscript{44} In 2001 the International Consensus Conference on NPPV in the acute setting concluded that, “the pathophysiology of conditions leading to hypercapnic... ARF is amenable to interventions available within the context of NPPV,” that there is a “physiologic rationale for the application of both inspiratory assistance and/or PEEP,” and that NPPV has “the potential of reducing the morbidity and possibly the mortality of hypercapnic respiratory failure.” However, the document cited “methodologic limitations [that] affect the interpretation of the current evidence.”\textsuperscript{45} These limitations included the use of small heterogeneous populations (which raised concerns about possible harm in subgroups even though the larger group showed benefit), the inability to adequately blind the studies so that bias could not be entirely excluded, and the conduct of most of the trials at centers of expertise, which raised concerns that the favorable results would not be reproducible at nonacademic sites.

More recently the British Thoracic Society issued a consensus statement on the use of NPPV for ARF. The statement recommended that NPPV be “considered in patients with a COPD exacerbation in whom a respiratory acidosis (pH $< 7.35$) persists despite maximum medical treatment on controlled oxygen therapy.”\textsuperscript{19}

Based on the current state of evidence and the favorable findings of multiple meta-analyses that selected only high-quality trials for analysis, I believe the case for using NPPV to treat COPD exacerbations is more compelling than is acknowledged in the consensus statements. Even allowing for the methodologic limitations, the studies have consistently shown highly significant favorable effects of NPPV in COPD exacerbations, though those results have not yet been replicated for other forms of ARF. Accordingly, I recommend that NPPV be considered the ventilatory modality of first choice to treat properly selected patients with COPD exacerbations and that this be considered a standard of care.

**NPPV to Treat Severe Stable COPD**

**Rationale for NPPV in the Long-Term Setting**

Despite the accumulating evidence to support the use of NPPV to treat COPD in the acute setting, the evidence regarding long-term NPPV for COPD is less compelling. Long-term NPPV for COPD was first described during the 1950s and 1960s, when tank ventilators were used to provide intermittent rest for some COPD patients.\textsuperscript{56} The mechanical disadvantages posed by hyperinflation in patients with advanced emphysema were summarized above. Dur-
ing the early 1980s investigators hypothesized that these mechanical disadvantages contributed to a state of chronic respiratory muscle fatigue in patients with severe COPD and that intermittent rest provided by NPPV would alleviate the fatigue, enhance respiratory muscle function between rest periods, and improve overall function and sense of well-being. This is referred to as the “muscle-resting hypothesis.”

An alternative but not necessarily mutually exclusive hypothesis has also been proposed, referred to here as the “sleep hypothesis.” This is based on the observation, derived from many investigations, that sleep quantity and quality are diminished in patients with severe COPD, compared to normal individuals. A corollary to this hypothesis is that sustained episodes of nocturnal hyperventilation can promote the retention of bicarbonate that blunts the respiratory center sensitivity to carbon dioxide. This could promote de novo or exacerbate pre-existing carbon dioxide retention, leading to a vicious cycle of carbon dioxide retention, more bicarbonate retention, and more carbon dioxide retention. These observations led investigators to hypothesize that nocturnal NPPV would ameliorate the sleep-disordered breathing, reduce the frequency of arousals, and permit longer and better quality sleep. As with enhanced respiratory muscle function, this would translate into an improved sense of well being and enhanced daytime functioning. Further, using the assisted ventilation at night might ameliorate nocturnal hyperventilation, permitting a resetting of the respiratory center sensitivity for carbon dioxide, and improving daytime ventilation.

**Testing the Muscle-Resting Hypothesis.** During the 1980s a number of studies tested the muscle-resting hypothesis. At the time, negative-pressure ventilation was the most commonly used mode of noninvasive ventilation, so most investigators used a version of negative-pressure ventilation referred to by a variety of monikers, including “poncho-wrap,” “jacket,” or “body suit” ventilator. This consisted of an impervious garment inside which a rigid cage was positioned over the chest and abdomen of the supine patient. The device assisted lung expansion when a negative-pressure pump intermittently created a negative pressure within the garment and the rigid cage prevented collapse of the garment.

Braun and Marino first tested the hypothesis with 16 severe-COPD patients and found improvements in vital capacity, maximum inspiratory and expiratory pressures, and daytime PaCO₂ after 5 months of 5 hours of daily “rest” provided by the “wrap” ventilator. Although this study was uncontrolled, it stimulated several controlled trials of negative-pressure ventilators, several of which yielded similar favorable findings, including improvements in maximum inspiratory and expiratory pressures and daytime gas exchange. However, these studies were only 3–7 days duration and were therefore too short to be relevant to the question of long-term NPPV for severe stable COPD.

Subsequent longer-term controlled trials, ranging from 3 weeks to 6 months, found no improvement in pulmonary function, maximum inspiratory or expiratory pressure, daytime arterial blood gas values, treadmill walking time, or subjective assessment of symptoms during noninvasive ventilation. In addition, they found that the wrap ventilator was poorly tolerated, with patients having difficulty sleeping during use and using it for fewer hours per day than recommended. These latter studies seemed to negate the hypothesis that muscle resting in COPD patients is useful and dampened enthusiasm for noninvasive ventilation in patients with severe stable COPD. However, the hypothesis could not be entirely rejected, because patient tolerance of the “wrap” ventilators was poor in most of the studies, raising the concern that it was poor adherence that prevented patients from realizing significant benefit. Notably, the average initial PaCO₂ among studies reporting favorable findings was 57 mm Hg, whereas the value was 47 mm Hg among the unfavorable studies. This suggests that the subgroup with severe stable COPD and severe hypercapnia may be the most likely to favorably respond to NPPV.

By the 1990s NPPV had replaced negative-pressure ventilation as the noninvasive modality of choice, by virtue of a number of advantages, including greater portability and convenience and the capability of treating rather than inducing obstructive sleep apnea. Investigators speculated that NPPV would be better tolerated and more efficacious than negative-pressure ventilation in providing ventilatory assistance to patients with severe stable COPD, but the results of subsequent controlled studies to examine that speculation have conflicted. Strumpf et al performed a 3-month cross-over trial using nasal NPPV with patients with severe stable COPD, but only neuropsychological function improved, not gas exchange, sleep variables, treadmill walking time, or symptoms. In contrast, Meecham-Jones et al in a similarly designed 3-month cross-over trial, observed improvements in total sleep time, daytime PaCO₂, and quality-of-life scores during use of NPPV. A notable difference between those studies that may offer an explanation for the conflicting findings is that patients in the Meecham-Jones et al study had both higher initial PaCO₂ (57 vs 47 mm Hg) and FEV₁ (821 vs 543 mL) and more nocturnal hypopneas than those in the Strumpf et al study. This suggests that hypercapnic patients, particularly those with at least some sleep-disordered breathing, may be the ones most likely to benefit from NPPV. The Strumpf et al study illustrated another problem frequently encountered in severe-COPD patients using NPPV: low adherence rates. Only seven of the 19 enrolled patients com-
completed the trial, with most dropping out or using the device for fewer than the recommended 5 hours per 24 hours.60

However, other controlled NPPV trials that have focused on hypercapnic (P\textsubscript{aCO\textsubscript{2}} > 50 mm Hg) patients failed to confirm the hypothesis that NPPV improves sleep in patients with severe stable COPD. In a 6-month trial Gay et al\textsuperscript{62} randomized 13 patients who had an average initial P\textsubscript{aCO\textsubscript{2}}, of 51 mm Hg to receive nasal NPPV or sham ventilation. Of the 7 patients who received NPPV, only four completed the trial and only one had a substantial reduction in daytime P\textsubscript{aCO\textsubscript{2}} (from 51 to 42 mm Hg). In view of the small number of patients, the failure to detect statistically significant differences is not surprising.

Lin\textsuperscript{63} subjected 12 severe stable COPD patients (average P\textsubscript{aCO\textsubscript{2}}, 51 mm Hg) to 4 conditions in randomized 2-week intervals: no oxygen or ventilatory assistance, oxygen supplementation alone, nasal ventilation alone, or the combination of oxygen and nasal ventilation. As expected, oxygenation improved during supplemental oxygen, but there were no improvements in pulmonary function, exercise capacity, or oxygenation attributable to NPPV, and total sleep time was significantly reduced during NPPV use. These unfavorable studies have been criticized for using relatively low inspiratory pressures that may have provided insufficient ventilatory assistance, small numbers of patients, and, in the case of the Lin study, inadequate study duration for successful adaptation to the nasal ventilator.

More recently, Casanova et al\textsuperscript{64} performed a year-long randomized trial with 44 hypercapnic patients with severe COPD and found no improvements in gas exchange or survival, although one measure of neuropsychological function improved.

In the most recent trial, Clini et al\textsuperscript{65} randomized 90 patients to receive, for 2 years, either oxygen therapy alone or oxygen therapy plus NPPV. Eight patients (of 43) dropped out of the NPPV arm, whereas fifteen (of 47) dropped out of the control arm, and eight died in each group. NPPV prevented the rise in P\textsubscript{aCO\textsubscript{2}} and decline in quality of life that were observed in controls. In addition, there was a strong trend toward fewer hospital days after initiation of NPPV (19 d vs 14 d, a non-significant difference). Six-minute walk distance, respiratory muscle strength, dyspnea, and sleep symptoms were unchanged. Although these studies were larger and longer than the prior studies and observed some benefits, neither study examined sleep duration or quality as an outcome variable.

In a multicenter European trial that began in 1992 and has been reported only in preliminary form thus far,\textsuperscript{66} 122 patients with an average P\textsubscript{aCO\textsubscript{2}}, of 56 mm Hg were randomized to receive NPPV or conventional therapy. As of the most recently reported abstract, there was no survival advantage in the NPPV group overall, but patients older than 65 years had significantly better survival.\textsuperscript{67}

Several uncontrolled studies have reported decreases in the frequency and duration of hospitalizations and ICU admissions after initiation of NPPV in patients with severe airway obstruction. In their retrospective studies, Leger et al\textsuperscript{68} and Jones et al\textsuperscript{69} found that hospital days per year fell from 49 and 16 days, respectively, for the year before starting NPPV, to 17 and 6 days for the year after. Along these lines, Vitacca et al\textsuperscript{70} found that ICU admissions for the year following acute NPPV treatment for COPD exacerbations averaged 0.12, compared to 0.3 for patients treated with invasive ventilation. These reductions may be related to stabilization of gas-exchange abnormalities or, alternatively, NPPV may enable patients to treat more COPD exacerbations at home by offering a means for patients to alleviate dyspnea.

Wijkstra et al\textsuperscript{71} recently performed a meta-analysis of studies examining the role of NPPV in patients with severe stable COPD. They reviewed 164 publications and 8 abstracts but included only 4 studies in their analysis, rejecting most because of lack of randomization, inadequate use of NPPV (< 5 h/night), or too short a training period (< 3 wk). Considering that three of the 4 studies selected for analysis were essentially negative (those by Strumpf et al,\textsuperscript{60} Gay et al,\textsuperscript{62} and Casanova et al,\textsuperscript{64} with the Meecham-Jones et al study\textsuperscript{65} being the only positive study), it is not surprising that the meta-analysis was inconclusive. The Clini et al study\textsuperscript{65} was excluded because it was not complete when the meta-analysis was performed. The only outcome variable with confidence intervals that excluded zero was maximum inspiratory pressure. The treatment effect for the 6-min walk test was large, but did not reach statistical significance. The authors concluded that the small sample sizes and other methodologic limitations of the studies in the meta-analysis “precluded a clear clinical direction” regarding the effects of NPPV on severe stable COPD, and that more large, well-designed trials are needed.

NPPV As an Adjunct to Exercise Training in Pulmonary Rehabilitation Programs. Another potential application of NPPV in patients with severe stable COPD is to enhance exercise training during rehabilitation. For example, when delivered via face mask during cycle ergometry, CPAP alone,\textsuperscript{72} pressure-support ventilation, and proportional-assist ventilation all reduce inspiratory effort and dyspnea in hypercapnic COPD patients.\textsuperscript{72} In a study that directly compared nasal CPAP, pressure-support ventilation, and proportional-assist ventilation in 15 patients with severe stable COPD (mean baseline P\textsubscript{aCO\textsubscript{2}}, 52 mm Hg), exercise duration on a cycle ergometer increased over baseline with all 3 ventilation modes, associated with significantly lower Borg dyspnea scores.\textsuperscript{72} Proportional-assist ventilation increased exercise duration more than the other modes, but the authors acknowledged that the titration methods used for the various modes differed, and they
refrained from drawing firm conclusions about relative effectiveness. These studies demonstrate that noninvasive modes can be used to increase or prolong the intensity of exercise training sessions in patients with severe COPD. Whether these effects translate into better overall function independent of ventilatory assistance at the completion of a rehabilitation program has not been established, however. One study that examined that question using proportional-assist ventilation as an adjunct to exercise training came up with negative findings.73

Another approach to combining NPPV with rehabilitation is to provide ventilatory assistance between rather than during exercise sessions. The theory is that the patient will thereby have better-rested respiratory muscles during exercise sessions and will function better. Garrod et al74 tested that hypothesis with 45 severe-COPD patients with mild or no hypercapnia treated with bi-level ventilation averaging 2 hours of every 24 hours. After 8 weeks of rehabilitation, the shuttle walk distance and Chronic Respiratory Disease Questionnaire scores were better in the NPPV patients than in controls, and the NPPV patients also had greater inspiratory strength (maximum inspiratory pressure $-66$ cm H$_2$O vs $-60$ cm H$_2$O in controls, $p < 0.05$). That finding is consistent with the idea that resting achieved by NPPV between exercise sessions enhances respiratory muscle function, but it is surprising that only 2 hours of NPPV per 24 hours achieves such benefit, and the finding needs to be confirmed in other studies.

**Summary of Potential Benefits of NPPV in Severe Stable COPD**

Although the available short-term controlled trials suggest that negative-pressure ventilation can improve respiratory muscle strength in these patients,54,55 no long-term controlled trials support this approach and NPPV should be considered the preferred ventilation technique. Benefits of NPPV supported by at least 2 controlled trials include increases in maximum inspiratory pressure and improvement (or at least prevention of deterioration) in nocturnal and daytime gas exchange, and better quality-of-life scores.61,65 Some evidence suggests that NPPV may increase walking distance,70 particularly if combined with rehabilitation.74 The studies examining effects on sleep have yielded some favorable findings, mainly prolongation of total sleep time in severely hypercapnic patients with some sleep-disordered breathing (average 10 hypopneas/h).61 However, other studies suggest that NPPV may interfere with sleep in less hypercapnic patients, particularly if they are not well acclimatized.63 Several uncontrolled studies67,68 and a trend in a controlled study65 suggest that NPPV reduces the need for hospitalization, which is an intriguing finding that deserves further study, particularly in view of the pressures in the United States to reduce hospital utilization, to contain health care costs. No convincing findings demonstrate a favorable effect of NPPV on survival, although a preliminary report of a controlled trial suggests benefit in an older subgroup.67 Clearly, NPPV has the potential to provide multiple benefits for patients with severe stable COPD, but with the methodological limitations of studies done thus far and the challenges of performing such studies in the future, the debate over the real benefits of NPPV for these patients is likely to continue for the foreseeable future.

**Selection of Patients with Severe Stable COPD to Receive NPPV**

**Consensus Guidelines.** Because of the conflicting data on the efficacy of NPPV in patients with severe stable COPD, the issue of patient selection has been controversial.75 On the one hand, very few longer-term controlled trials have shown any benefit, a number of other controlled trials have shown no benefit, and pending the results of further studies, it can be argued that NPPV is unjustified for severe stable COPD. On the other hand, the studies with unfavorable findings had methodological shortcomings, a number of uncontrolled trials have suggested benefit, and the lack of confirmatory controlled trials should not be used as a justification for withholding entirely what may be an effective therapy for some patients.

In response partly to this conundrum and partly to the rapidly increasing use of NPPV with COPD patients, sometimes for questionable indications, that occurred in 1997, the Durable Medical Equipment Reimbursement Commission of the United States Health Care Financing Admin-

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**Table 3. Guidelines for Use of NPPV in Severe Stable COPD**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic after optimal therapy</td>
<td>Symptomatic after optimal therapy</td>
</tr>
<tr>
<td>Sleep apnea excluded</td>
<td>Sleep apnea excluded</td>
</tr>
<tr>
<td>$P_{ACO_2} \geq 55$ mm Hg or</td>
<td>$P_{ACO_2} \geq 55$ mm Hg or</td>
</tr>
<tr>
<td>$P_{ACO_2} 50-54$ mm Hg and evidence of nocturnal hypoventilation</td>
<td>$P_{ACO_2} 50-54$ mm Hg and evidence of nocturnal hypoventilation</td>
</tr>
<tr>
<td>based on nocturnal oximetry showing sustained desaturation to $&lt;89%$ for $\geq 5$ min while patient is on his or her usual $FI_{O_2}$</td>
<td>based on nocturnal oximetry showing sustained desaturation to $&lt;89%$ for $\geq 5$ min while patient is on his or her usual $FI_{O_2}$</td>
</tr>
<tr>
<td>Repeated hospitalizations</td>
<td>Repeated hospitalizations</td>
</tr>
<tr>
<td>Evidence of nocturnal hypoventilation based on nocturnal oximetry showing sustained desaturation to $&lt;89%$ for $\geq 5$ min while patient is on his or her usual $FI_{O_2}$</td>
<td>Evidence of nocturnal hypoventilation based on nocturnal oximetry showing sustained desaturation to $&lt;89%$ for $\geq 5$ min while patient is on his or her usual $FI_{O_2}$</td>
</tr>
<tr>
<td>Sleep apnea excluded clinically (polysomnogram not required)</td>
<td>Sleep apnea excluded clinically (polysomnogram not required)</td>
</tr>
<tr>
<td>Requisite 3-month initial trial of bilevel device without a back-up rate</td>
<td>Requisite 3-month initial trial of bilevel device without a back-up rate</td>
</tr>
</tbody>
</table>

NPPV = noninvasive positive-pressure ventilation
COPD = chronic obstructive pulmonary disease
$FI_{O_2} =$ fraction of inspired oxygen
*Adapted from Reference 76.
istration (recently renamed the Centers for Medicare and Medicaid Services [CMS]) requested in 1998 that the National Association for Medical Direction of Respiratory Care and the American College of Chest Physicians convene a consensus group of medical experts to suggest guidelines for the use of NPPV in severe stable COPD that could be incorporated into CMS guidelines. Based on a review of the pertinent literature and the observation that, almost without exception, studies reporting favorable responses to NPPV among patients with severe stable COPD were conducted with severely hypercapnic patients, the consensus group opined that a trial of NPPV was justified with a symptomatic but stable and optimally treated patient who has daytime $P_{aCO_2} \geq 55$ mm Hg, if obstructive sleep apnea had been excluded (Table 3). For $P_{aCO_2}$ between 50 and 54 mm Hg, the group suggested that there should be evidence of worsening hypoventilation during sleep, as suggested by a sustained (> 5 min) desaturation during use of the usual oxygen supplementation. In addition, the need for repeated hospitalizations was deemed a justification for a trial of NPPV.\textsuperscript{76}

CMS guidelines based on the consensus group recommendations and modified in response to suggestions from clinicians, home respiratory care vendors, and ventilator manufacturers are also presented in Table 3. The main differences between the consensus recommendations and CMS guidelines are that $P_{aCO_2} \geq 52$ mm Hg is required and sustained oxygen desaturation during oxygen supplementation must be demonstrated, regardless of the $P_{aCO_2}$ value. The consensus group had opined that evidence of sustained desaturation was unnecessary if $P_{aCO_2}$ exceeded 55 mm Hg. The CMS guidelines also do not recognize repeated hospitalizations as an indication for long-term mechanical ventilation. In addition, the CMS guidelines require a 3-month trial of ventilatory assistance without a back-up rate. The requirements that sustained nocturnal desaturations be documented and that a ventilator without a back-up rate be tried for the first 3 months have led to a drastic reduction in the use of NPPV for severe stable COPD.

**Contraindications to NPPV for COPD**

In addition to the selection guidelines discussed above, other factors should be considered when selecting patients (Table 4). NPPV relies on the patient’s ability to protect the airway, so swallowing dysfunction, excessive secretions, and cough impairment are relative contraindications to NPPV. In addition, successful adaptation to NPPV may be a lengthy and taxing process, particularly in COPD patients, among whom acceptance rates tend to be lower than among patients with restrictive thoracic disorders.\textsuperscript{77} Hence, lack of motivation or noncompliance with medication or oxygen therapy are also relative contraindications to NPPV. Further, patients with cognitive defects or an inability to understand the therapy are poor candidates. Inability to fit a mask is an obvious contraindication to use, and some patients lack the financial or caregiver resources needed for NPPV, particularly in the home.

**Practical Application of NPPV for COPD Patients**

A thorough discussion of the application of NPPV is beyond the scope of this article, and the reader is referred to complete descriptions.\textsuperscript{2,78} The following sections focus on applications with COPD patients.

**Initiation**

Techniques for initiation are similar in both the acute and chronic settings and must be tailored for each individual patient. Of course, the level of urgency is greater in the acute setting, necessitating rapid selection of a mask and ventilator, so all equipment, including masks, ventilators, tubing, and humidifiers should be readily available. It may be helpful to attach to the NPPV cart a “mask bag” containing various types and sizes of masks and straps. With long-term NPPV, mask adjustments and mask changes can be made over days or weeks rather than minutes. In either setting experienced practitioners who can impart a sense of confidence and reassurance should implement NPPV.

**Mask Selection**

In the acute setting the full face (oronasal) mask is usually the preferred initial choice because it controls mouth leaks better than nasal masks.\textsuperscript{79} Patients rate nasal masks as more comfortable for long-term applications,\textsuperscript{80} so transitioning from an oronasal to a nasal mask should be contemplated after the first few days if NPPV is to be continued. Masks should be optimally fitted using fitting

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Table 4. Relative Contraindications to Long-Term NPPV for COPD Patients

| Severe comorbidity that is likely to shorten survival more than lung disease (end-stage malignancy, liver disease). Congestive heart failure may respond favorably. |
| Unmotivated patient |
| Nonadherent to oxygen or medical therapy |
| Cognitive impairment that interferes with patient’s ability to understand therapy |
| Insufficient financial resources |
| Insufficient caregiver resources |
| Unable to tolerate or fit mask; claustrophobic patient |

NPPV = noninvasive positive-pressure ventilation
COPD = chronic obstructive pulmonary disease
gauges, if provided by the manufacturer. Too large a mask may necessitate excessive tightening of the straps to minimize air leakage, predisposing to ulceration over the nose. Many types of nasal and oronasal mask are now available, including nasal pillows or plugs (small cones that fit directly into the nares), “minimasks” that fit over just the tip of the nose, masks with gel seals or with thin, ultrasoft silicone seals. The headgear (ie, the straps that hold the mask in place) are also important in achieving comfort. They should have sufficient points of attachment (usually ≥ 3) to maintain mask stability, although for long-term use some “minimasks” with 2 points of attachment may function adequately. When tightened, they should minimize air leakage, especially into the eyes, but should still accommodate 1 or 2 fingers between the strap and face, to avoid excessive tightening. Practitioners should have a current knowledge of available masks in order to optimize the likelihood of success.

**Ventilator Selection**

In the acute setting, both critical care and bi-level ventilators (portable pressure-limited devices designed especially for the administration of NPPV) have been used with similar success rates, although bi-level devices designed for use in the acute care setting that offer oxygen blenders and display waveforms are gaining popularity. In the long-term setting bi-level ventilators are also seeing increasing use, although portable volume-limited ventilators are still used for some patients because of their greater alarm capabilities.

**Ventilator Settings**

To begin NPPV the properly-fitted mask is placed on the patient’s face and attached to the ventilator. Cooperative patients often feel more comfortable if they hold the mask themselves. Initial ventilator pressures are usually set low, to enhance patient comfort and acceptance, but inspiratory pressure or tidal volume should be adjusted upward as tolerated to provide adequate ventilatory assistance. Typical initial settings on pressure-limited ventilators are 8–12 cm H2O for inspiratory pressure and 4–5 cm H2O for expiratory pressure or PEEP, with subsequent adjustments as needed to alleviate respiratory distress (increased inspiratory pressure up to 20 cm H2O) or to counterbalance auto-PEEP, treat hypoxemia, or eliminate obstructive apneas (increased expiratory pressure up to 8 cm H2O). The difference between the inspiratory and expiratory positive airway pressure (pressure support) should be adequate to reduce ventilatory effort and is usually between 7 and 16 cm H2O, adjusted to alleviate respiratory distress while avoiding excessive discomfort.

Coaching is usually necessary to assist the patient in achieving synchrony with the ventilator, but once this is achieved, the head straps can be tightened. Some ventilators offer further adjustments to enhance synchrony, including adjustable inspiratory time and rise time, which determines the time to reach the target inspiratory pressure. These may be helpful in optimizing comfort for patients who prefer relatively high inspiratory flow and hence short rise time (often 0.1 s) and short inspiratory time (often < 1 s) to avoid “hang-up” (the prolongation of delivered inspiratory pressure during expiration).

**Oxygenation and Humidification**

Most patients with COPD exacerbations do not have severe oxygenation defects and can be managed successfully with bi-level ventilators that do not have oxygen blenders. With these ventilators oxygen is administered at up to 15 L/min into ports in the mask or via a T-piece at the proximal end of the ventilator tubing, adjusted to maintain the desired level of oxygenation (usually saturation > 90–92%). With this arrangement FIO2 does not exceed 45–50%, so a ventilator with an oxygen blender is necessary when the oxygenation defect is more severe, such as may occur when COPD is complicated by pneumonia. Humidification may enhance comfort and tolerance during NPPV, but heat-and-moisture exchangers may add to resistance and should be avoided. With bi-level ventilators, heated pass-over humidifiers are recommended because they offer efficiency of humidification without adding substantially to inspiratory or expiratory resistance.

**Adaptation and Monitoring**

In the acute setting, the first hour or two are critical in achieving successful NPPV adaptation. Coaching and encouragement are usually required to assist the patient in adopting a breathing pattern that achieves synchronization with the ventilator and reduction of breathing effort and, if nasal ventilation is being used, in keeping the mouth shut. Instructions such as “try to take slow, deep breaths and let the machine breathe for you” may be helpful. Also, judicious administration of low doses of sedatives such as midazolam may be helpful in enhancing patient acceptance. In the chronic setting, the time course is drawn out, but an initial session in the physician’s office or even in the hospital, if possible, may be helpful in determining which mask is most acceptable and comfortable for the patient, what settings are best tolerated, and perhaps most important in COPD patients, in assuring that the patient is well motivated for an adaptation period that may be lengthy.

In the acute setting, close bedside monitoring is essential until the patient’s respiratory status stabilizes. Although NPPV can easily be administered on a general medical
ward, the acuteness of the illness and need for close monitoring should dictate the site of administration. With either invasive or noninvasive ventilation, an acutely ill patient should be treated in an intensive care or step-down unit until his or her condition stabilizes. Patient comfort and tolerance are key initial goals (Table 5). In a COPD patient a decrease in respiratory rate and reduction in sternocleidomastoid muscle activity are important salutary signs that should be apparent early on and are usually accompanied by good patient-ventilator synchrony. Upward adjustments in inspiratory pressure enhance these effects. Oxygen saturation is monitored continuously and blood gas values are obtained as clinically indicated, usually at least once during the first hour or two.

With long-term NPPV, adaptation usually requires much longer than in the acute setting, mainly because the patient attempts to sleep while using the ventilator. The patient is instructed to initiate NPPV at home for 1- or 2-hour trial periods during the daytime and then to try to fall asleep with the device at bedtime. During this period frequent contact with an experienced home respiratory therapist (RT) can help assure proper use and adjustment. Some patients successfully sleep through the night within days of initiation, but others require several months. But even when begun under ideal conditions, COPD patients’ NPPV adherence may be relatively low. Criner et al found that only 50% of COPD patients were still using NPPV after 6 months, compared to 80% for neuromuscular patients, even after initiating NPPV during a 3-week stay in a skilled long-term ventilation unit. Reasons for poor adherence have not been well studied but probably include the advanced age of COPD patients (compared to neuromuscular-disease patients), frequent occurrence of comorbidities and cognitive defects, and lack of motivation. For these reasons, close follow-up is probably helpful to optimize compliance rates. The supplier of home respiratory equipment should provide respiratory care services as well, so that patients can be in telephone contact with questions, and RTs should make frequent (at least weekly) initial visits. A physician should see the patient every few weeks during the initial adaptation period, to assess symptoms and physical signs for evidence of persisting nocturnal hypventilation or cor pulmonale, identify problems, and reinforce adherence. Occasionally measuring daytime arterial blood gas values helps to assess the response in hypventilating patients or when symptoms worsen. Nocturnal monitoring using oximetry, multichannel recorders, or full polysomnography is also useful after adaptation to NPPV, to assure adequacy of oxygenation and ventilation.

### Commonly Encountered Problems and Possible Remedies

NPPV is safe and well tolerated in most properly selected patients. In both the acute and long-term applications the most commonly encountered NPPV problems with COPD patients are similar to those with other patients and are related to the mask or air pressure or flow. Patients often complain of mask discomfort, which can be alleviated by minimizing strap tension or trying different mask sizes or types. With acute applications, patients may be anxious and have difficulty synchronizing their breathing with the ventilator. Adjustments in ventilator settings (increasing or lowering inspiratory pressure, or titrating expiratory pressure to counter-balance auto-PEEP) and judicious use of sedation often will improve synchrony.

Excessive air pressure leading to sinus or ear pain is another common complaint, alleviated by lowering pressure temporarily and then gradually raising it again as tolerance improves. Patients may also complain of dryness or congestion of the nose or mouth. For dryness, nasal saline or gel, heated flow-by humidifier, or efforts to reduce air leaking may help. For nasal congestion, inhaled corticosteroids or decongestants or oral antihistamine-decongestant combinations may be used.

Other commonly encountered problems include erythema, pain, or ulceration on the bridge of the nose related to pressure from the mask seal; these can be alleviated by minimizing strap tension, using artificial skin, or switching to alternative masks such as nasal pillows. Gastric insufflation is common but usually not severe, probably because inflation pressures are lower than those used with invasive ventilation.

### Table 5. Monitoring NPPV in COPD

<table>
<thead>
<tr>
<th>Acute Setting</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient comfort</td>
<td>Patient comfort</td>
</tr>
<tr>
<td>Mask fit and leak</td>
<td>Mask fit and leak</td>
</tr>
<tr>
<td>Patient-ventilator synchrony</td>
<td>Patient-ventilator synchrony</td>
</tr>
<tr>
<td>Sternocleidomastoid muscle activity</td>
<td>Sternocleidomastoid muscle activity</td>
</tr>
<tr>
<td>Vital signs: heart and respiratory rate, systemic blood pressure</td>
<td>Vital signs: heart and respiratory rate, systemic blood pressure</td>
</tr>
<tr>
<td>Continuous oximetry until stabilized</td>
<td>Continuous oximetry until stabilized</td>
</tr>
<tr>
<td>Occasional blood gas measurements: initial and after 30–120 min, then as clinically indicated</td>
<td>Occasional blood gas measurements: initial and after 30–120 min, then as clinically indicated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic Setting</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient comfort</td>
<td>Patient comfort</td>
</tr>
<tr>
<td>Mask fit and leak</td>
<td>Mask fit and leak</td>
</tr>
<tr>
<td>Hours of use</td>
<td>Hours of use</td>
</tr>
<tr>
<td>Problems with adaptation (eg, nasal congestion, dryness, gastric insufflation, conjunctival irritation, inability to sleep)</td>
<td>Problems with adaptation (eg, nasal congestion, dryness, gastric insufflation, conjunctival irritation, inability to sleep)</td>
</tr>
<tr>
<td>Symptoms (eg, dyspnea, fatigue, morning headache, hypersomnolence)</td>
<td>Symptoms (eg, dyspnea, fatigue, morning headache, hypersomnolence)</td>
</tr>
<tr>
<td>Gas exchange: daytime, nocturnal oximetry, blood gases measured periodically to assess $P_{\text{aco}_2}$</td>
<td>Gas exchange: daytime, nocturnal oximetry, blood gases measured periodically to assess $P_{\text{aco}_2}$</td>
</tr>
<tr>
<td>Polysomnography if symptoms of sleep disturbance persist or nocturnal desaturation persists without clear explanation</td>
<td>Polysomnography if symptoms of sleep disturbance persist or nocturnal desaturation persists without clear explanation</td>
</tr>
</tbody>
</table>

NPPV = noninvasive positive-pressure ventilation  
COPD = chronic obstructive pulmonary disease
Air leaking, through the mouth (with nasal masks), through the nose (with mouthpieces), or around the mask (with all interfaces), is inevitable during NPPV. Nasal and oronasal masks, particularly if too large, may leak air onto the eyes, causing conjunctival irritation. Refitting or re-seating the mask usually addresses this problem. Pressure-limited devices compensate for air leaks by maintaining inspiratory airflow during leaking, but during nasal ventilation the patient should keep his or her mouth shut and try chin straps or, failing these, try an oronasal mask. Air leaking occurs during the majority of sleep in many patients but, fortunately, gas exchange is usually well maintained. Leaks may still contribute to arousals and poor sleep quality, however, and ventilatory assistance may occasionally be compromised, in which case options include trials of alternative interfaces or ventilators, or if those fail, tracheostomy. Major complications of NPPV, such as aspiration or pneumothorax, are unusual if patient selection guidelines are observed.

Role of the Respiratory Therapist

NPPV has become an important part of the RT’s repertoire. In the United States and Italy, the RT maintains and applies the equipment necessary to initiate NPPV. The RT also devotes substantial time (up to an hour or more) during the initial 8-hour shift in applying NPPV, as compared to invasive mechanical ventilation. NPPV requires a team approach, with the physician determining when NPPV is appropriate and ordering it. Nurses, at least in the acute setting, provide ongoing monitoring once NPPV has been initiated. But the RT plays the critical part of initiating NPPV, getting the patient’s cooperation, and successfully sustaining it. Without skilled, experienced RTs to serve that role a successful NPPV program cannot be implemented.

Summary

Accumulating evidence and experience have demonstrated that NPPV has an important role in managing COPD exacerbations, markedly reducing the need for intubation and improving outcomes, including lowering complication and mortality rates, as well as shortening hospital stay. For COPD exacerbations NPPV should now be considered a standard of care for properly selected patients, used in preference to invasive mechanical ventilation. NPPV can also be used in certain other situations with COPD patients: when respiratory failure is precipitated by a superimposed pneumonia, in postoperative respiratory failure, to facilitate extubation with the aim of reducing the complications of prolonged intubation, to avoid reintubation in patients with postextubation failure, and in do-not-intubate patients, although the evidence to support these applications is not as strong as for NPPV in typical COPD exacerbations. To assure appropriate use of NPPV for these patients, selection guidelines are aimed at identifying patients in need of ventilatory assistance and excluding those who are too ill to safely use NPPV. Although these have not been validated prospectively, they are based on criteria used in most of the controlled trials.

For patients with severe stable COPD, currently available evidence suggests that NPPV can improve daytime and nocturnal gas exchange, prolong sleep duration, improve quality-of-life scores, and possibly reduce the need for hospitalization. However, the findings among studies have not been consistent on these benefits, partly related to numerous methodological shortcomings in most studies performed to date. Despite the weakness of the evidence base, however, consensus and CMS guidelines agree that COPD patients with substantial daytime carbon dioxide retention and evidence of superimposed nocturnal hypoventilation are the ones most likely to benefit. However, it is also clear that more confirmatory studies are needed before the use of NPPV in any group of COPD patients can be considered established practice; even with sufficient evidence, it is likely that achieving desired NPPV adherence by COPD patients will remain a challenge. Ultimately, the test of any therapy is whether caregivers find it useful and beneficial in their own practices, and by that criterion the jury is still out on the question of how widely NPPV should be used in patients with severe COPD.

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Discus: In our study of noninvasive ventilation given at home as an adjunct to rehabilitation, the overall usage of the ventilator was quite low.1 The problem was that some of the patients did not take ventilators for 2–3 days at a stretch and this pushed down the median number. Overall, if you look at the time that they actually took the ventilator, the use was between 3 and 4 hours. I think that is interesting because I have a number of patients with hypercapnic COPD who I know are not taking their home ventilators for more than about 2 to 3 hours a day. The blood gas values stabilize and the patients feel better and reduce the usage of the ventilator. I am impressed with the improvements some patients had in that trial.

In a study of this nature, placebo effects must be considered, as sham ventilation is difficult to perform. However, bearing that in mind, I think there is an effect of the combination of the ventilation and exercise training, but it is small. You probably do not need to give 6 or 8 hours of ventilation overnight. You may be able to get away with a much smaller amount of ventilation.

REFERENCE


Hill: Do you use NPPV in combination with pulmonary rehabilitation now?

Wedzicha: We do not. A number of patients in that study continued to use it. However, in the UK, patients with hypercapnic COPD are treated with home ventilatory support if they deteriorate on oxygen therapy or have sleep disruption or uncontrolled hypercapnia. However, the evidence is not perfect, and although there have been many discussions over the years about this, there has been no study adequately powered for study of the effects of nasal ventilation on mortality. However, indeed, I feel that the most important effect of ventilation is on reduction in exacerbation as we have found improvements in health status after ventilatory support in hypercapnic COPD.1 Exacerbations worsen blood gases, and then the NPPV will reduce the consequences of the exacerbation. The problem we have is that such trials need to be multicenter and are difficult to organize.

REFERENCE


Hill: Both Wisia [Wedzicha] and I have made efforts to do the kind of trial that would be necessary, and a number of you know the travails I’ve been through with this, but the National Institutes of Health has not been convinced that I can recruit enough patients and maintain their adherence. They look at Gerry Criner’s data and say, “You know, the power analysis you’re giving us doesn’t look too convincing when you might have a 50% dropout rate.” So that’s been a major problem with coming up with good evidence on the use of NPPV in severe, stable COPD patients.

REFERENCE


Wedzicha: Just one more point about the dropout rate. The way we cut it down in the study by Meecham-Jones et al was to test everybody on NPPV beforehand.1 The RT tests whether the patient can accept the NPPV and “passes” or “fails” the patient. I think you need some form of patient selection. I believe that in the United States you have enough patients to do these trials, even allowing for dropouts.

REFERENCE

Gay: You could put a different spin on Criner’s data, and I’ll just offer this to you, as we’ve started a protocol on this at the Mayo Clinic. To the extent that these patients drop out because they get better and they don’t need it any more, it may be a misguided conclusion to look at it as a failure rather than a completion of NPPV therapy. I think it’s not appropriate to look at long-term NPPV as a dreaded therapy. These patients were coming out of acute respiratory failure and were being moved quickly out of the critical care unit within 2 days, to make room for sicker patients. This leaves these patients in limbo as to whether they need to continue NPPV out of ICU and out of hospital. Recognizing that continued long-term NPPV therapy after 1 year following COPD exacerbation is not supported by currently-available literature, such as from Casanova et al,[1] it doesn’t reflect upon the fact that a short-term benefit may be present. In that study there was a significant reduction in readmission to hospital in the first 3 months. Wouldn’t it be valuable to look at that aspect of it, saying, “Give them something for a month or 2 and see if they get better. If they stop it, hey, that’s not necessarily a bad thing if they stabilized enough to stop.”

Hansen-Flaschen: I think all of us think that NPPV is here to stay as one element of the armamentarium in inpatient care of COPD exacerbations. I’d like to see more attention turn now to the experience of the patient who is undergoing mechanical ventilation in that setting. In a previous Respiratory Care Journal Conference,[1] I made an argument for patient-centered mechanical ventilation, by which I meant simply the addition (to the physiologic variables that we usually measure while administering mechanical ventilation) of one question to the patient, and that is, “Are you feeling short of breath right now?” If the person says yes the therapist ought to make some effort to reduce the shortness of breath, either by adjusting the ventilator or getting help from a nurse or a physician. I’m not aware of any routine NPPV protocols that include the question to the conscious, communicative patient, “Are you feeling short of breath right now?” I wonder if you would comment on that.

REFERENCE


Hill: That is something that’s been looked at in a number of the randomized, controlled trials, at least compared to the control group. Both Wisia [Wedzicha] and I have data showing that NPPV reduces dyspnea more rapidly than conventional mechanical ventilation. Of course, there may be some residual dyspnea. Also, when you’re making adjustments to NPPV there are competing aims: one is to alleviate respiratory distress and the other is to avoid discomfort related to excessive pressure or flow. Sometimes you have to make compromises where the patient will have a little residual dyspnea, but at least he won’t feel like the machine’s blowing his eardrums out. So we’re limited in what we can do.

Hansen-Flaschen: My proposal is simply to have respiratory therapists add to every bedside visit the question, “Are you feeling short of breath right now?” and maybe, “Is the mask uncomfortable right now?” That can be recorded as a yes or no, along with the physiologic variables, as a discipline of including the patient and the patient’s experience in the adjustment and monitoring of the treatment.

Hill: What I’m saying is that what we really need to think about is optimizing the patient’s overall comfort rather than only dyspnea, because dyspnea is only one part of it. Mask and air pressure discomfort are other aspects of getting the patient comfortable.

Benditt: I want to bring up do-not-intubate patients. Having worked a lot in palliative care of patients with neuromuscular disease and other diseases, I believe that NPPV is quite underutilized. There are good data that it reduces dyspnea, and at the end of life it actually may provide more time for closure of affairs. It reduces dyspnea and it does not have the so-called “double effect” that morphine does, of relieving symptoms but potentially shortening life. I’m a strong advocate for NPPV, although there is, in fact, a lot of resistance to it; for instance some people believe it is equivalent to intubation. I think it’s quite different and potentially very beneficial.
If the mask is just annoying them and making them obviously more uncomfortable, you can always stop NPPV, and perhaps that’s the kind of proviso we should use.

**Stoller:** My question regards the hospital venue in which NPPV ought to be used for patients suffering COPD exacerbations and mild hypercapnia. You cited the Plant study,1 which was done not in the ICU but on the ward, and it showed mortality benefit. In the United States we’re confronted with a glut of patients admitted to the general medical ward with mild hypercapnia and who may or may not go to the ICU; they usually don’t, which raises the question of NPPV on the ward and what are the outcome metrics? What are the possibilities if things do not go well on the ward? Does one then admit the patient to the ICU in a flurry of activity without airway availability? I’ve had conversations that suggest that this is a common problem that many of us face. With patients who have pH of 7.29 or 7.31 and acute-on-chronic ventilatory failure, do we admit them to the intensive care unit for 24 hours to initiate NPPV and avert intubation, and then move them on to the ward? Or do we admit them to the general medical ward and hope that most of them escape intubation, and with those who don’t, we have this flurry of activity and move them to the ICU?

**Hill:** That’s an issue that creates problems in almost every hospital where NPPV is used, and of course the answer depends on the hospital’s resources. I take a pragmatic approach to this. I don’t think you can use hard rules, but you can probably come up with soft guidelines with regard to pH and P\textsubscript{CO\textsubscript{2}}. My view is that it really boils down to how long it takes for your patient to get into trouble when the mask falls off. With hypoxemic patients, it’s often a matter of minutes, and the mask has to go right back on. That’s a patient who clearly needs very close observation. On the other hand, some patients improve rapidly in the emergency room, and you can take the mask off for 20 or 30 minutes and nothing happens. I would argue that that patient probably can be observed safely on a regular medical floor, as long as there’s every reason to think that the patient will remain otherwise stable.

**Gay:** Can I follow up on that? We ran into the problem of showing quick success out of the emergency room with a battery-powered NPPV device. Our emergency department is very adept at this. We adapted a battery to a bi-level portable device, and we get them up in the unit quickly. This process enchanted the ward staff with using NPPV, but it’s a tremendous consumption of resources—which is the other end of the spectrum. It got to the point that we had to limit the use of NPPV on the ward and say, “Look, if you’re going to use NPPV for acute respiratory failure, you have to understand that this is not a trivial intervention. This is not just oxygen therapy.” And to make an RT set this up means it’s not just something to make the patient feel better for a little while. It’s an acute intervention. So we’ve greatly limited the initiation of NPPV on the ward; we want initiation in a much more structured environment.

**Hill:** Jamie Stoller’s question was about assessing the patient’s need for monitoring. If the need is high, then the patient should go to the intensive care unit. I don’t think it’s right to have a guideline saying that every NPPV patient needs to go to the ICU. I think that would lead to inappropriate utilization of resources.

**REFERENCE**