

Noninvasive positive pressure ventilation in the intensive care unit: A concise review

Sean M. Caples, DO; Peter C. Gay, MD

Objective: To critically assess available high-level clinical studies regarding use of noninvasive positive pressure ventilation in varied intensive care unit settings.

Data Source: Search of pertinent articles within Ovid MEDLINE from 1975 to 2005, CINAHL from 1982 to 2005, EMBASE from 1988 to 2005, and Web of Science from 1993 to 2005.

Study Selection: Randomized, controlled clinical trials and cohort studies and observational studies the authors consider important or novel.

Data Extraction/Synthesis: Performed equally by both authors with the use of an Excel data spreadsheet.

Conclusion: There is abundant level I evidence supporting the use of noninvasive positive pressure ventilation in such critical

care settings as acute hypercapnic respiratory failure, particularly related to chronic obstructive pulmonary disease, and acute cardiogenic pulmonary edema. We also report on other clinical scenarios in which the data may be somewhat less compelling, but evidence favors a noninvasive positive pressure ventilation trial. Some well designed studies suggest that noninvasive positive pressure ventilation is not an appropriate intervention for patients who have failed endotracheal extubation. (Crit Care Med 2005; 33:2651–2658)

KEY WORDS: noninvasive positive pressure ventilation; acute respiratory failure; hypercapnic respiratory failure; positive airway pressure; mechanical ventilation

Noninvasive positive pressure ventilation (NPPV) therapy is increasingly popular in varied clinical situations in the intensive care unit (ICU) setting as high-level evidence supporting its use continues to accumulate. The attraction for NPPV relates primarily to its advantages over invasive mechanical ventilation. It has been shown to comparatively decrease resource utilization and circumvents the myriad of complications associated with invasive mechanical ventilation such as upper airway trauma, ventilator-associated pneumonia, and compromise of speech and swallowing. NPPV should, however, be considered an alternative to invasive mechanical ventilation rather than its replacement. Keys to the success of NPPV and to improving clinical outcomes of patients with acute respiratory failure are careful patient selection and a well designed clinical protocol because failure of NPPV only delays potentially

more definitive therapy with invasive ventilation.

NPPV can be delivered using various types of ventilatory equipment and interfaces. Full-service ICU ventilators, portable bi-level pressure generators, and devices specifically designed to be used for NPPV are now available (1). The complete details of the application of NPPV are beyond the scope of this review, but virtually any ventilator, mode, and interface techniques may be used successfully, as briefly alluded to in Figure 1. The determinants of success are less dependent on these technical factors and relate more prominently to the primary diagnosis as discussed below.

Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) are among the most frequently encountered in the critical care setting with acute respiratory failure. Physiologic studies consistently demonstrate that NPPV improves variables such as PCO_2 , PO_2 , and respiratory rate in these patients (2–4), and there are data that quantify the degree of respiratory muscle unloading associated with NPPV (5).

The burden of disease associated with acute exacerbations of COPD is reflected

in the large number of randomized, controlled clinical trials (RCTs) studying NPPV in these patients, either as the sole disease state or as a subgroup. The earliest study came from Bott et al. (6) in 1993, which randomized 60 patients to either volume-controlled NPPV by nasal mask or conventional treatment. Significant improvements were noted in the treatment group compared with controls in such variables as PCO_2 , pH, and dyspnea scores. Although 30-day mortality was higher in the control group (30% vs. 10%), statistical significance was not reached with an intention-to-treat analysis, probably because of the relatively small number of patients.

Subsequent RCTs have demonstrated the indisputable efficacy of NPPV in acute exacerbations of COPD utilizing other delivery methods such as pressure support ventilation and bilevel assist ventilation by nasal or oronasal masks. The use of standardized protocols for NPPV treatment initiation and specific indications for endotracheal intubation for treatment failure, by reducing reliance on clinical judgment, have helped to limit the introduction of bias. Two studies are worthy of further mention. A 1995 multiple-center ICU study by Brochard et al. (3) randomized 85 patients from a larger group of 275 with COPD to pressure support ven-

From the Division of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine, Rochester, MN.

The authors have no financial interests to disclose. Copyright © 2005 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/01.CCM.0000186768.61570.69

RESPIRATORY THERAPY DRIVEN PROTOCOL FOR CPAP AND NIV USE IN ACUTE RESPIRATORY FAILURE (ARF)

I. Patient Evaluation

- Review history, diagnosis, inclusion, exclusion criteria and discuss with MD
- Ascertain whether new NIV use or an accustomed patient
- Assess for component of chronic respiratory failure

II. Indications and Goals

- Choose as per patient diagnosis, level of distress, and whether ICU based
- Decide options in event of early benefit or poor initial response
- Reaffirm code status and patient preferences regarding alternative therapy

III. Location

- Determine observation and monitoring needs per patient condition and equipment used (a step-down unit may be appropriate for single organ failure or patients clearly recovering from multi-organ failure).

IV. Equipment: Conditions, Initial Settings, and Targets

- Airflow generator
- 1. **CPAP.** Presumed obstructive sleep apnea or cardiogenic ARF for target of improved SpO₂ and PaCO₂
- 2. **Portable Bi-Level Device.** Acute on chronic component for target of improved PaCO₂ and reduced dyspnea using visual analog scale. Use with portable battery attachment for transporting patients.
- 3. **ICU Bi-Level Device.** Choose for patients in ICU, more severe distress in emergency department, or poor synchrony and need for waveform monitoring
- 4. **Full Service ICU ventilator.** Severely distressed patients with poor synchrony in consideration of pressure or volume control modes
- Settings
 1. **CPAP.** set at 10-12.5 cmH₂O and titrate as needed for OSA or dyspnea
 2. **Portable Bi-Level Device.** Initial EPAP at minimum for neuromuscular disease patients, 5 cmH₂O for others. May increase EPAP for OSA component or for hypoxemia. Attention to auto-PEEP, which may be counteracted by judicious use of EPAP. Initial IPAP at 8-10cmH₂O and target patient tolerance. Increase to 15-20cmH₂O as tolerance allows for relief of dyspnea and respiratory rate.
 3. **ICU Bi-Level Device.** Same EPAP and IPAP issues as for portable device but may need more aggressive titration as situation demands. Alter flow rate, sensitivity, and inspiratory time to optimize synchrony.
 4. **Full Service ICU Ventilator.** Same issues as for ICU Bi-level device but may consider use of volume control and other modes.
 5. **Oxygen.** Guided by distress level and SpO₂. In those at risk of worsening hypercapnia on CPAP, maintain between 88%-90%
- Masks
 1. **Nasal.** Utilize for less distressed patients and those with chronic component. Also consider nasal pillows for more claustrophobic patients
 2. **Full Face Mask.** Patients with severe distress or large oral air leaks

V. Monitoring

- Oximetry. All patients.
- Arterial Blood Gases. Baseline and discharge ABGs highly recommended. Useful for ICU patients needing frequent monitoring of PaCO₂
- Ventilator with waveform monitoring for poor synchrony problems

VI. Dismissal (Education and Communication)

- Anticipate early for patients with chronic component
- Review for diagnostic and reimbursement requirements

VII. NIV registry/oximetry (recommended but not obligatory)

- Documentation. Log progress and outcome for future patient use and protocol quality assessment

*Reproduced from Gay, PC, Hubmayr, RD: "Mechanical ventilation part II: noninvasive." In Irwin and Rippe's *Intensive Care Medicine* 5th ed. 2003. p. 647-60.

Figure 1. Respiratory therapy-driven protocol for continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV) use in acute respiratory failure (ARF). ICU, intensive care unit; EPAP, expiratory positive airway pressure; PEEP, positive end-expiratory pressure; IPAP, inspiratory positive airway pressure; ABGs, arterial blood gases; OSA, obstructive sleep apnea; NNV, noninvasive nasal ventilation.

tilation by face mask vs. usual care. Although there were only small reductions in Pco₂ in the treatment group, between-group differences in endotracheal intubation, complications, and mortality were substantial, resulting in some criticism of the adequacy of treatment in the control group. Still, this study highlighted the importance of careful patient selection for NPPV.

Another important study, the largest RCT (n = 236) of NPPV in acute exacerbations of COPD to date, originated from 14 hospitals in the UK (7). Control patients had significantly higher rates of endotracheal intubation (27%) compared with NPPV-treated patients (15%). All patients were cared for on general respiratory wards rather than in the ICU, which may have factored into the higher mortality rates noted in those with a baseline pH < 7.30. These results may not be generalizable, however, due to the unique structure of respiratory care delivery by trained nursing staff in the UK. Follow-up analyses of data that showed improvements in pH and respiratory rate over the initial 4 hrs of NPPV conferred success of treatment (8) and confirmed substantial cost savings as a result of treatment outside of the ICU (9). The initial response to NPPV has consistently been shown to be a strong predictor of success, as noted below.

One RCT found no significant difference in primary outcomes related to NPPV when compared with controls (10). Four of 24 randomized patients did not tolerate nasal bi-level ventilation, and no patient in either group deteriorated to require endotracheal intubation. The lack of intubations, plus the mild degree of respiratory acidosis in these patients at baseline (mean pH of 7.33), supports the widely accepted notion that ideally suited patients for treatment with NPPV are those with more severe acute exacerbations of COPD with hypercapnia. Indeed, in a subgroup analysis of a systematic review of RCTs by Keenan et al. (11), there was little to support the benefit of NPPV in milder exacerbations of COPD. Further confirmation comes from a recently updated Cochrane Database Systematic Review that included 14 RCTs enrolling 758 patients with a baseline Pco₂ of >45 mm Hg showing significant improvements in intubation rate, complications, length of hospital stay, and mortality associated with NPPV treatment (12). From these study results, treatment of hypercapnic patients with acute exac-

erbatation of COPD can generally be expected to reduce intubation rates, mortality, and ICU or hospital length of stay (Table 1).

Acute Cardiogenic Pulmonary Edema

Acute cardiogenic pulmonary edema may be treated effectively with continuous positive airway pressure (CPAP). CPAP does not exert its primary effect on ventilation per se, but its efficacy in counteracting the pathophysiologic pathways in cardiogenic pulmonary edema has long been recognized, described as early as 1936 (13). Delivery of positive end-expiratory pressure opens flooded or collapsed alveoli, thereby increasing functional residual capacity and improving gas exchange. There seem to be direct mechanical effects on the heart and great thoracic vessels attributed to CPAP, resulting in reductions of cardiac afterload and cardiac wall stress. Finally, CPAP reduces the work of breathing, in part by overcoming upper airway resistance, which may be increased by soft-tissue edema seen in association with heart failure (14, 15). Indeed, a number of clinical trials have demonstrated the efficacy of CPAP in improving oxygenation and circumventing endotracheal intubation in cardiogenic pulmonary edema when compared with controls largely treated with supplemental oxygen (16–18).

Given the improvements attributable to CPAP in this population, it would stand to reason that NPPV would also have similar effects. In fact, two case series published simultaneously, consisting of 55 patients collectively, suggested that NPPV (pressure support ventilation) improved gas exchange and rates of invasive mechanical ventilation (19, 20). However, seven deaths from myocardial infarction raised concern about the use of NPPV in patients with myocardial ischemia. Similar apprehension came from a 1997 study, the first published trial randomizing CPAP against bi-level NPPV in cardiogenic pulmonary edema encountered in the emergency department (ED) setting (21). Enrollment was terminated after 27 patients because of the high rate of myocardial infarction in the NPPV group (71% vs. 31% in the CPAP group), although significantly more patients with chest pain were allocated to NPPV, suggesting a compromised randomization schedule.

The increased risk of myocardial infarction and death attributed to NPPV has not been substantiated in more recent RCTs. A 40-patient ICU-based study utilizing tidal volume adjustment and pressure support compared with oxygen plus medical therapy showed a reduced rate of endotracheal intubation (5% vs. 33%) and reduced resolution time of respiratory failure (30 vs. 105 mins), as determined by objective measurements, attributed to NPPV (22). Mortality and hospital length of stay were no different. A larger (130 patients randomized) multiple-center study from Italy, initiating treatment in the ED, although demonstrating improvements in $\text{PaO}_2/\text{FIO}_2$ ratios and dyspnea, showed a reduction in tracheal intubation rates only in the subgroup of patients with hypercapnia (23). Conceivably, the lack of benefit to other patients could be due to the relative lack of ED personnel experience with the use of NPPV compared with their ICU colleagues and that ventilatory strategy in this protocol was not tidal volume driven. The question is important, however, because early institution of CPAP or NPPV, which may optimally occur in the ED, seems to promote avoidance of invasive mechanical ventilation. An attempt to answer this question came from a study originating in two UK EDs that randomized 60 patients (from an eligible pool of 236) with respiratory acidosis and cardiogenic pulmonary edema to fixed-pressure CPAP (10 cm H_2O), bilevel NPPV (inspiration = 15, expiration = 5), or oxygen therapy (24). The protocol was limited to 2 hrs of randomized treatment in the ED. Predetermined determinants of treatment success at 2 hrs, including endotracheal intubation rates, were no different between the three groups. For reasons that are unclear, in-hospital mortality was significantly higher in the bilevel and control groups compared with the CPAP group. Although the authors attributed survival benefit to CPAP therapy, the evidence supporting that conclusion is weak. Collectively considering the available data, the treatment of acute cardiogenic pulmonary edema with respiratory compromise should include early application of CPAP. In the presence of hypercapnia, NPPV may be more appropriate.

Hypoxemic Respiratory Failure

Historically, despite occasional case reports of success, hypoxemic respiratory failure (excluding COPD) has been

thought to be poorly responsive to NPPV therapy. Among the first RCTs to demonstrate this came from a study by Wysocki et al. (25) in which 41 non-COPD patients were randomized to NPPV or oxygen. The results showed that only those with a Paco_2 of >45 mm Hg had positive outcomes in terms of endotracheal intubation and ICU length of stay. Given the heterogeneity in severity of illness commonly encountered in pure hypoxemic respiratory failure, such as encountered in acute respiratory distress syndrome, these findings may not be entirely unexpected. It should be noted that CPAP also has been shown to be of little benefit in preventing endotracheal intubation in a trial of 123 patients with pulmonary edema largely due to acute respiratory distress syndrome or acute lung injury (26).

Other studies, however, suggest that selected patients with hypoxemic respiratory failure may benefit from NPPV. Antonelli et al. (27) compared NPPV with conventional invasive mechanical ventilation in 64 patients with varied causes of hypoxemic respiratory failure, including cardiogenic pulmonary edema but excluding COPD. Those ventilated noninvasively had significantly lower rates of serious complications, including pneumonia and sinusitis, and shorter total ventilation time and ICU length of stay. A multiple-center study from Spain of 105 patients with severe hypoxemia from varied causes, other than COPD, resulted in ICU and 90-day survival benefit and reduced rates of invasive ventilation and septic shock for the group randomized to NPPV compared with those treated with high-flow oxygen by Venturi mask (28). Thus, there is limited evidence supporting the use of NPPV in hypoxemic respiratory failure. In the setting of single organ (respiratory) failure, we believe a trial of NPPV is warranted, with the caveat that endotracheal intubation should not be delayed if rapid improvement in gas exchange indices does not occur or there is instability of extrapulmonary clinical variables.

Postoperative Respiratory Failure

Studies of respiratory failure in the postoperative setting have shown favorable results from both NPPV and CPAP. Nearly a decade ago, Joris et al. (29) demonstrated improvement in pulmonary function in obese patients after gastroplasty, a finding that remains important

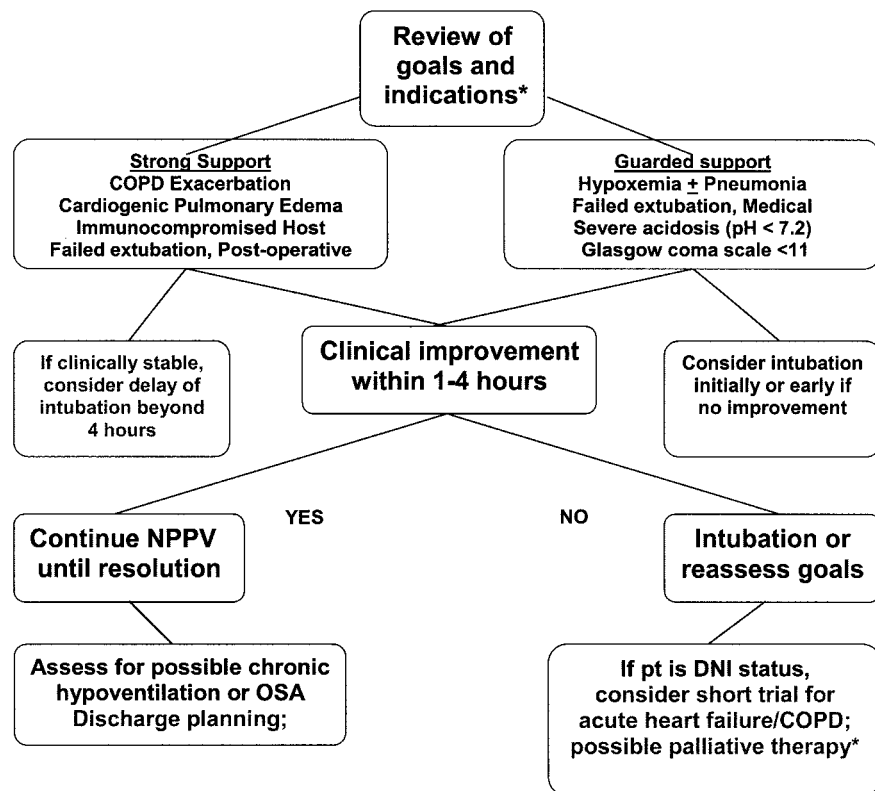
Table 1. Randomized controlled trials of noninvasive positive pressure ventilation (NPPV)^a

Study, Year (Reference No.)	Population	Site	Intervention		Sample Size		Study Design		Results (Effect of NPPV)			
			NPPV	Control	NPPV	Control	Co-intervention Standardized	Intubation Criteria Standardized	ETI or Failure Criteria	Mortality	Physiology Improved	Complic
Bersten et al., 1991 (17)	ACPE	ED-ICU	CPAP	UMC	19	20	No	Yes	↓	↔	Yes	NR
Bott et al., 1993 (6)	COPD	Ward	ACV	UMC	30	30	No	No	↓	↓ ^b	Yes	NR
Wysocki et al., 1995 (25)	ARF (no COPD)	ICU	PSV + PEEP	UMC	21	20	Yes	Yes	↔	↔	NR	↔
Brochard et al., 1995 (3)	COPD	ICU	PSV	UMC	43	42	Yes	Yes	↓	↓	Yes	↓
Kramer et al., 1995 (2)	ARF	ICU	IPAP + EPAP	UMC	16	15	No	Yes	↓	↔	Yes	↔
Barbe et al., 1996 (10)	COPD	Ward	IPAP + EPAP	UMC	20	20	Yes	No	↔	↔	Yes	NR
Mehta et al., 1997 (21)	ACPE	ED-ICU	IPAP + EPAP	CPAP	14	13	Yes	No	↔	↔	Yes	↑ ^c
Nava et al., 2003 (23)	COPD Weaning	ICU	PSV + PEEP	PSV + PEEP Invasive	25	25	No	Yes	NR	↓	Yes	↓
Celikel et al., 1998 (4)	COPD	ICU	PSV + PEEP	UMC	15	15	Yes	No	↓ ^d	↔	Yes	NR
Antonelli et al., 1998 (27)	AHRF	ICU	PSV + CPAP	ACV + PEEP, SIMV + PSV + PEEP	32	32	Yes	Yes	↓ ^e	↔	Yes	↓
Wood et al., 1998 (27a)	ARF, AHRF	ED	IPAP + EPAP	UMC	16	11	No	Yes	↔	↔	No	↔
Confalonieri et al., 1999 (35)	CAP + ARF, AHRF	Intermed care	PSV + CPAP	UMC	28	28	No	Yes	↓	↔	Yes	↔
Girault et al., 1999 (35a)	ARF Weaning	ICU	PSV + PEEP	PSV + PEEP (invasive)	17	16	No	Yes	↔	↔	Yes	↔
Jiang et al., 1999 (35b)	Postextubation	ICU	IPAP + EPAP	UMC	47	46	No	No	↔	↔	NR	NR
Antonelli et al., 2000 (32)	ARF Solid organ transplantation	ICU	PSV + PEEP	UMC	20	20	Yes	Yes	↓	↓ ^f	Yes	↓
Martin et al., 2000 (33a)	ARF, AHRF	ICU	IPAP + EPAP	UMC	32	29	No	No	↓	↔	NR	↔
Plant et al., 2000 (7)	COPD	Ward	Pressure Cycled	UMC	118	118	Yes	Yes	↓	↓	NR	NR
Delclaux et al., 2000 (26)	AHRF (non-hypercapnic)	ICU	CPAP	UMC	62	61	Yes	Yes	↔	↔	Yes	↑
Masip et al., 2000 (22)	ACPE	ICU	PSV + CPAP	UMC	20	20	Yes	Yes	↓	↔	Yes	NR
Auriant et al., 2001 (31)	AHRF Post-op	ICU	IPAP + EPAP	UMC	24	24	Yes	Yes	↓	↓	Yes	NR
Hilbert et al., 2001 (33)	AHRF Immunosupp	ICU	PSV + CPAP	UMC	26	26	Yes	Yes	↓	↓	Yes	↓
Levitt et al., 2001 (49)	ACPE	ED	IPAP + EPAP	UMC	19	19	No	No	↔	↔	No	NR
Keenan et al., 2002 (42)	ARF, AHRF Weaning	ICU	IPAP + EPAP	UMC	39	42	Yes	Yes	↔	↔	NR	NR
Conti et al., 2002 (50)	ARF	ICU	PSV + CPAP	ACV + PEEP, PSV + PEEP	23	26	Yes	Yes	↔	↔	Yes	↔
Ferrer et al., 2003 (28)	AHRF	ICU	IPAP + EPAP	UMC	51	54	Yes	Yes	↓	↓	Yes	↓
L'Her et al., 2004 (51)	ACPE Elderly (>75 yrs old)	ED	CPAP	UMC	43	46	Yes	Yes	↓	↔	Yes	↓
Esteban et al., 2004 (43)	ARF, AHRF Weaning	ICU	PSV + CPAP	UMC	114	107	Yes	Yes	↔	↑	NR	NR
Squadrone et al., 2005 (30)	AHRF Post-op	ICU	CPAP	UMC	105	104	Yes	Yes	↓	↔	Yes	↓

ETI, endotracheal intubation; ↓, decreased after NIV; ↑, increased after NIV; ↔, no change after NIV; Complic, complications (e.g., pneumonia); ACPE, acute cardiogenic pulmonary edema; ED, emergency department; ICU, intensive care unit; CPAP, continuous positive airway pressure; UMC, usual or standard medical care; NR, not reported; COPD, chronic obstructive pulmonary disease; ACV, assist control (volume-cycled) ventilation; ARF, acute hypercapnic respiratory failure; PSV, pressure support ventilation; PEEP, positive end-expiratory pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive pressure; Weaning, studies that used NPPV to facilitate weaning from mechanical ventilation; AHRF, acute hypoxemic respiratory failure; SIMV, spontaneous intermittent mandatory ventilation; intermed care, intermediate respiratory care unit; postextubation, studies using NPPV to prevent reintubation after extubation; immunosupp, immunosuppressed.

^aModified from Gay PC, Hubmayr RD: Mechanical ventilation part II: Noninvasive. *In*: Irwin and Rippe's Intensive Care Medicine. Fifth Edition. Irwin RS, Rippe JM (Eds). Philadelphia, Lippincott Williams and Wilkins, 2003, pp 647–660; ^bafter exclusion of four patients who did not tolerate NPPV (no difference in mortality with intention-to-treat analysis); ^cincreased incidence of myocardial infarction; ^dpatients in the control group who required NPPV after satisfying failure criteria; ^eall patients in the control group were intubated; ^fICU mortality (no difference noted in hospital mortality).

NPPV for Acute Respiratory Failure



***Discussion with patient must include frank explanation that NPPV should be considered aggressive respiratory support that may not be consistent with patient prior directives. Each patient situation requires addressing individual specific wishes and needs as NPPV is also reasonable as a palliative treatment.**

Figure 2. Noninvasive positive pressure ventilation (NPPV) for acute respiratory failure. COPD, chronic obstructive pulmonary disease; *pt*, patient; *DNI*, do not intubate; *OSA*, obstructive sleep apnea.

today given the sharp increases in rates of obesity surgeries nationwide. Mediated primarily by lung atelectasis, hypoxemia is relatively common after abdominal surgery. A recent large Italian study was stopped early due to improvements in intubation rates related to CPAP therapy in hypoxemia after abdominal surgery, an effect that is probably mediated in part through reversal of atelectasis (30). In a nonblinded study, the use of NPPV in patients with hypoxemic respiratory failure after lung resection resulted in a reduced need for invasive mechanical ventilation (21% vs. 50%) and lower mortality rates (12.5% vs. 37.5%) when compared with oxygen therapy, although some of the benefit may have derived from the high rate of pulmonary edema in each group (31). In those patients who develop hypoxemic respiratory failure after uncomplicated elective abdominal

surgery, CPAP should be considered early as a means to reduce the need for endotracheal intubation. There are fewer data in the setting of other surgeries, but with single organ failure after otherwise uncomplicated procedures, including lung resection, CPAP or NPPV is a reasonable therapeutic option.

Immunocompromised Patients

Avoidance of the infectious complications associated with invasive mechanical ventilation is particularly appealing in immunocompromised patients, in whom this could be devastating, if not fatal. Two revealing articles have demonstrated the benefit of NPPV in this population. Antonelli et al. (32) randomized 40 solid organ transplant recipients to NPPV or oxygen for hypoxemic respiratory failure, the cause of which was acute respiratory

distress syndrome in nearly half. Improvements associated with NPPV included decreases in rates of endotracheal intubation, fatal complications, ICU mortality, and length of stay. A second study assessed the use of NPPV in 52 neutropenic patients with pulmonary infiltrates and hypoxemic respiratory failure (more than half due to hematologic malignancy and chemotherapy) (33). NPPV resulted in fewer intubations and serious complications and reduced ICU and hospital mortality. Of particular importance to the success of NPPV, as demonstrated in these studies, is careful patient selection. Multiple organ failure, frequently encountered in this setting, was an exclusion criterion, and judging by the average use of NPPV of only 7 to 9 hrs per 24 hrs, the respiratory failure was relatively mild. This notwithstanding, it is still reasonable to consider NPPV as initial ventilatory therapy in the immunocompromised patient (34).

Pneumonia, Severe Acute Respiratory Syndrome (SARS)

Although it is possible that some of the immunosuppressed patients in the studies above indeed had infectious pneumonia, the evidence to support the use of NPPV specifically for pneumonia is sparse. Confalonieri et al. (35) performed a randomized trial of NPPV vs. oxygen therapy in 56 patients (23 of whom had underlying COPD) with severe community-acquired pneumonia. Although there was a modest benefit afforded the NPPV group in regard to intubation and ICU stay, 60-day survival improved only in those patients with COPD. The same group of investigators showed improved outcomes in a nonrandomized clinical series of AIDS patients with severe pneumocystis pneumonia treated with NPPV compared with those who were invasively ventilated (36). The available evidence suggests that, particularly in the presence of hypercapnia, patients with other forms of infectious pneumonia may benefit from NPPV.

A retrospective study reported the Hong Kong experience with NPPV during the severe acute respiratory syndrome (SARS) outbreak (37). A total of 20 patients (19 with positive coronavirus serology) were treated with NPPV for respiratory failure consistent with SARS. Although they were young (mean age, 51 yrs) and had Acute Physiology and Chronic Health Evaluation II scores of

only 5.35, 30% of the patients still needed endotracheal intubation. Although the selected patients and methodology may overestimate benefit from NPPV, it is noteworthy that none of the 105 health-care workers caring for these patients developed active signs of infection. Given the unclear efficacy of NPPV in other forms of hypoxemic respiratory failure, caution should be observed when considering this therapy for SARS patients. Although air exhaled from ventilators with dual lumen circuits can be filtered, concern for caregiver safety should remain high in SARS patients given the highly contagious nature of this disease.

Facilitation of Weaning from Invasive Mechanical Ventilation/Rescue of Failed Extubation (Not Postoperatively)

It is well known that the need for re-intubation after failed extubation is associated with poor outcomes and higher mortality than for those patients successfully extubated, even after adjustment for severity of underlying illness (38, 39). Uncontrolled studies have reported improvements in physiologic variables and reduced need for re-intubation in patients treated with NPPV after failed initial extubation from invasive mechanical ventilation (40, 41). Although this was studied predominantly in those with COPD, there seemed to be adequate proof of concept that this could be considered a reasonable intervention to avoid reintubation. In response to a call from an international consensus conference for randomized, controlled trials to further assess this, two articles were recently published that, to the surprise of many, showed no benefit from NPPV (42, 43). In fact, the larger, multiple-center trial was terminated early after an interim analysis of the first 221 patients revealed a significantly higher mortality rate in the NPPV group (42). An important observation of this study showed that the time from respiratory failure to re-intubation was much longer in the NPPV group (12 hrs) than the standard therapy group (2.5 hrs), underscoring the effect of prompt institution of definitive therapy, whether it be NPPV or invasive mechanical ventilation. Because the number of patients with COPD was small in both studies by design, it is premature to generalize these results to those with COPD who fail extubation because, as noted above, there is evidence (albeit of lower strength) to

support the use of NPPV in these patients. The findings from the above clinical trials should not necessarily preclude a trial of NPPV in non-COPD patients who fail extubation but draws attention to the importance of early and frequent reassessment for signs of NPPV failure and timely endotracheal re-intubation. Standardized guidelines or protocols for patient selection and management may be useful, as discussed below.

Asthma and Other Conditions

Although large RCTs assessing the utility of NPPV in the setting of acute asthma are lacking, the ability of NPPV to unload the respiratory muscles could conceivably avert endotracheal intubation in some patients with status asthmaticus. Small studies have shown some benefit in this setting (44, 45). Similar caveats apply to this and other conditions in which NPPV may be of use, such as acute respiratory failure in the setting of obesity-hypoventilation syndrome, where reassessment for progressive respiratory failure and depressed level of consciousness should be early and frequent, so as not to delay endotracheal intubation if needed.

Patient Selection and Summary

As stated previously, the success of NPPV is critically dependent on careful patient selection. There is strong evidence that patients with COPD respond well to NPPV, particularly under certain conditions. Predictors of success include younger age, unimpaired consciousness, moderate rather than severe hypercarbia and acidemia, and prompt physiologic response (improvement in heart and respiratory rates and gas exchange within 2 hrs) (46). Confalonieri et al. (47) recently published a logistic regression model to predict failure of NPPV in patients with acute exacerbations of COPD. Based on 1,033 consecutive COPD patients, of whom 236 (22.8%) failed NPPV, the model showed the highest risk for failure occurred in those with a Glasgow coma scale of <11, pH < 7.25, and a respiratory rate of >30 breaths/min.

Based on the findings reported above, we have designed an algorithm for NPPV and urge the use of established institutional protocols that are subjected to frequent reassessment. Studies often emphasize disease indications and the initiation process for NPPV but are per-

There is abundant level I evidence supporting the use of noninvasive positive pressure ventilation in such critical care settings as acute hypercapnic respiratory failure, particularly related to chronic obstructive pulmonary disease, and acute cardiogenic pulmonary edema.

haps lacking in statements regarding response to failure and less appropriate use of NPPV. For this reason, we insist on careful discussion of the goals and preferences of the patient and practitioners before initiating NPPV treatment. We regard NPPV as aggressive therapy and do not initiate this on the hospital ward or in patients who have clear directives against more advanced respiratory supportive therapy. However, a "do not resuscitate or intubate (DNR/DNI)" order should not itself preclude a trial of NPPV, which, as Levy et al. (48) recently showed, can be associated with a favorable outcome in the setting of an acute event such as congestive heart failure or COPD exacerbation. In other settings of respiratory failure in DNR/DNI patients, NPPV may enhance patient comfort by reducing the work of breathing and may be appropriate for short-term use (49–51). However, fully informed consent should leave no ambiguity that NPPV could prolong a terminal event.

We support a team approach to the delivery of NPPV that involves respiratory therapists and nursing staff, and we have found that a worksheet performs well in our practice (Fig. 1). Once the goals, location, and equipment choices are made, a generalized approach to treatment can follow a logical progression (Fig. 2). Finally, we have designed a database to track general use of this therapy for future reassessment that will support continued research involving equipment, technique, and patient selection.

REFERENCES

1. Hill NS: Noninvasive Positive Pressure Ventilation: Principles and Applications. Armonk, NY, Futura Publishing Company, 2001
2. Kramer N, Meyer TJ, Meharg J, et al: Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure [see comment]. *Am J Respir Crit Care Med* 1995; 151:1799–1806
3. Brochard L, Mancebo J, Wysocki M, et al: Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease [see comment]. *N Engl J Med* 1995; 333:817–822
4. Celikel T, Sungur M, Ceyhan B, et al: Comparison of noninvasive positive pressure ventilation with standard medical therapy in hypercapnic acute respiratory failure. *Chest* 1998; 114:1636–1642
5. Wysocki M, Richard JC, Meshaka P: Noninvasive proportional assist ventilation compared with noninvasive pressure support ventilation in hypercapnic acute respiratory failure. *Crit Care Med* 2002; 30:323–329
6. Bott J, Carroll MP, Conway JH, et al: Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet* 1993; 341:1555–1557
7. Plant PK, Owen JL, Elliott MW: Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: A multicentre randomised controlled trial [see comment]. *Lancet* 2000; 355:1931–1935
8. Plant PK, Owen JL, Elliott MW: Non-invasive ventilation in acute exacerbations of chronic obstructive pulmonary disease: Long term survival and predictors of in-hospital outcome [see comment]. *Thorax* 2001; 56:708–712
9. Plant PK, Owen JL, Parrott S, et al: Cost effectiveness of ward based non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease: Economic analysis of randomised controlled trial. *BMJ* 2003; 326:956–959
10. Barbe F, Togoires B, Rubi M, et al: Noninvasive ventilatory support does not facilitate recovery from acute respiratory failure in chronic obstructive pulmonary disease. *Eur Respir J* 1996; 9:1240–1245
11. Keenan SP, Sinuff T, Cook DJ, et al: Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. *Ann Intern Med* 2003; 138:861–870
12. Ram FS, Picot J, Lightowler J, et al: Noninvasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease [update of *Cochrane Database Syst Rev* 2003; 1:CD004104]. *Cochrane Database Syst Rev* 2004; 1:CD004104
13. Poulton E: Left-sided heart failure with pulmonary edema: Its treatment with the “pulmonary plus pressure machine.” *Lancet* 1936; 2:981–983
14. Shepard J Jr, Pevernagie D, Stanson A, et al: Effects of changes in central venous pressure on upper airway size in patients with obstructive sleep apnea. *Am J Respir Crit Care Med* 1996; 153:250–254
15. Yap JCH, Moore DM, Cleland JGF, et al: Effect of supine posture on respiratory mechanics in chronic left ventricular failure. *Am J Respir Crit Care Med* 2000; 162:1285–1291
16. Rasanen J, Heikkila J, Downs J, et al: Continuous positive airway pressure by face mask in acute cardiogenic pulmonary edema. *Am J Cardiol* 1985; 55:296–300
17. Bersten AD, Holt AW, Vedig AE, et al: Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991; 325:1825–1830
18. Lin M, Yang Y, Chiang H, et al: Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary edema: Short-term results and long-term follow-up. *Chest* 1995; 107:1379–1386
19. Hoffmann B, Welte T: The use of noninvasive pressure support ventilation for severe respiratory insufficiency due to pulmonary oedema. *Intensive Care Med* 1999; 25:15–20
20. Rusterholtz T, Kempf J, Berton C, et al: Noninvasive pressure support ventilation (NIPSV) with face mask in patients with acute cardiogenic pulmonary edema (ACPE) [see comment]. *Intensive Care Med* 1999; 25:21–28
21. Mehta S, Jay GD, Woolard RH, et al: Randomized, prospective trial of bilevel versus continuous positive airway pressure in acute pulmonary edema. *Crit Care Med* 1997; 25:620–628
22. Masip J, Betbese AJ, Paez J, et al: Noninvasive pressure support ventilation versus conventional oxygen therapy in acute cardiogenic pulmonary oedema: A randomised trial. *Lancet* 2000; 356(Suppl):2126–2132
23. Nava S, Carbone G, DiBattista N, et al: Noninvasive ventilation in cardiogenic pulmonary edema: A multicenter randomized trial. *Am J Respir Crit Care Med* 2003; 168:1432–1437
24. Crane SD, Elliott MW, Gilligan P, et al: Randomised controlled comparison of continuous positive airways pressure, bilevel noninvasive ventilation, and standard treatment in emergency department patients with acute cardiogenic pulmonary oedema. *Emerg Med J* 2004; 21:155–161
25. Wysocki M, Tric L, Wolff MA, et al: Noninvasive pressure support ventilation in patients with acute respiratory failure: A randomized comparison with conventional therapy. *Chest* 1995; 107:761–768
26. Delclaux C, L’Her E, Alberti C, et al: Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: A randomized controlled trial [see comment]. *JAMA* 2000; 284:2352–2360
27. Antonelli M, Conti G, Rocco M, et al: A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure [see comment]. *N Engl J Med* 1998; 339:429–435
- 27a. Wood KA, Lewis L, Von Harz B, et al: The use of noninvasive positive pressure ventilation in the emergency department. *Chest* 1998; 113:1339–1346
28. Ferrer M, Esquinas A, Leon M, et al: Noninvasive ventilation in severe hypoxemic respiratory failure: A randomized clinical trial. *Am J Respir Crit Care Med* 2003; 168:1438–1444
29. Joris J, Sottiaux T, Chiche J, et al: Effect of bi-level positive airway pressure (BiPAP) nasal ventilation on the postoperative pulmonary restrictive syndrome in obese patients undergoing gastropasty. *Chest* 1997; 111:665–670
30. Squadrone V, Coia M, Cerutti E, et al: Continuous positive airway pressure for treatment of postoperative hypoxemia: A randomized controlled trial. *JAMA* 2005; 293:589–595
31. Auriant I, Jallot A, Herve P, et al: Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. *Am J Respir Crit Care Med* 2001; 164:1231–1235
32. Antonelli M, Conti G, Bufi M, et al: Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: A randomized trial. *JAMA* 2000; 283:235–241
33. Hilbert G, Gruson D, Vargas F, et al: Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure [see comment]. *N Engl J Med* 2001; 344:481–487
- 33a. Martin TJ, Hovis JD, Costantino JP, et al: A randomized, prospective evaluation of noninvasive ventilation for acute respiratory failure. *Am J Respir Crit Care Med* 2000; 161:807–813
34. Hill NS: Noninvasive ventilation for immunocompromised patients. *N Engl J Med* 2001; 344:522–524
35. Confalonieri M, Potena A, Carbone G, et al: Acute respiratory failure in patients with severe community-acquired pneumonia: A prospective randomized evaluation of noninvasive ventilation [see comment]. *Am J Respir Crit Care Med* 1999; 160(5 Pt 1):1585–1591
- 35a. Girault C, Daudenthun I, Chevron V, et al: Noninvasive ventilation as a systematic extubation and weaning technique in acute-on-chronic respiratory failure: A prospective, randomized controlled study. *Am J Respir Crit Care Med* 1999; 160:86–92
- 35b. Jiang J-S, Kao S-J, Wang S-N: Effect of early application of biphasic positive airway pressure on the outcome of extubation in ventilator weaning. *Respirology* 1999; 4:161–165
36. Confalonieri M, Calderini E, Terraciano S, et al: Noninvasive ventilation for treating acute respiratory failure in AIDS patients with *Pneumocystis carinii* pneumonia. *Intensive Care Med* 2002; 28:1233–1238
37. Cheung TM, Yam LY, So LK, et al: Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome [see comment]. *Chest* 2004; 126:845–850

38. Epstein SK, Ciubotaru RL, Wong JB: Effect of failed extubation on the outcome of mechanical ventilation. *Chest* 1997; 112: 186–192
39. Epstein SK, Ciubotaru RL: Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. *Am J Respir Crit Care Med* 1998; 158:489–493
40. Kilger E, Briegel J, Haller M, et al: Effects of noninvasive positive pressure ventilatory support in non-COPD patients with acute respiratory insufficiency after early extubation [see comment]. *Intensive Care Med* 1999; 25:1374–1380
41. Hilbert G, Gruson D, Portel L, et al: Noninvasive pressure support ventilation in COPD patients with postextubation hypercapnic respiratory insufficiency. *Eur Respir J* 1998; 11:1349–1353
42. Keenan SP, Powers C, McCormack DG, et al: Noninvasive positive-pressure ventilation for postextubation respiratory distress: A randomized controlled trial [see comment]. *JAMA* 2002; 287:3238–3244
43. Esteban A, Frutos-Vivar F, Ferguson ND, et al: Noninvasive positive-pressure ventilation for respiratory failure after extubation [see comment]. *N Engl J Med* 2004; 350: 2452–2460
44. Soroksky A, Stav D, Shpirer I: A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. *Chest* 2003; 123: 1018–1025
45. Meduri GU, Cook TR, Turner RE, et al: Noninvasive positive pressure ventilation in status asthmaticus. *Chest* 1996; 110:767–774
46. Mehta S, Hill NS: Noninvasive ventilation. *Am J Respir Crit Care Med* 2001; 163: 540–577
47. Confalonieri M, Garuti G, Cattaruzza MS, et al: A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. *Eur Respir J* 2005; 25:348–355
48. Levy M, Tanios MA, Nelson D, et al: Outcomes of patients with do-not-intubate orders treated with noninvasive ventilation. *Crit Care Med* 2004; 32:2002–2007
49. Levitt MA: A prospective, randomized trial of BiPAP in severe acute congestive heart failure [see comment]. *J Emerg Med* 2001; 21: 363–369
50. Conti G, Antonelli M, Navalesi P, et al: Noninvasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: A randomized trial [see comment]. *Intensive Care Med* 2002; 28:1701–1707
51. L'Her E, Duquesne F, Girou E, et al: Noninvasive continuous positive airway pressure in elderly cardiogenic pulmonary edema patients. *Intensive Care Med* 2004; 30:882–888