The Use of Noninvasive Positive Pressure Ventilation in the Emergency Department*

Results of a Randomized Clinical Trial

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Objective: To determine whether the use of noninvasive positive pressure ventilation (NPPV) in the emergency department (ED) will reduce the need for tracheal intubation and mechanical ventilation.

Design: Randomized, controlled, prospective clinical trial.

Setting: ED of Barnes-Jewish Hospital, a university-affiliated teaching hospital.

Patients: Twenty-seven patients meeting a predetermined definition of acute respiratory distress requiring hospital admission.

Interventions: Conventional medical therapy for the various etiologies of acute respiratory distress and the application of NPPV.

Measurements and results: The primary outcome measure was the need for tracheal intubation and mechanical ventilation. Secondary outcomes also assessed included hospital mortality, hospital length of stay, acquired organ system derangements, and the utilization of respiratory care personnel. Sixteen patients (59.3%) were randomly assigned to receive conventional medical therapy plus NPPV, and 11 patients (40.7%) were randomly assigned to receive conventional medical therapy without NPPV. The two groups were similar at the time of randomization in the ED with regard to demographic characteristics, hospital admission diagnoses, and severity of illness. Tracheal intubation and mechanical ventilation was required in seven patients (43.8%) receiving conventional medical therapy plus NPPV and in five patients (45.5%) receiving conventional medical therapy alone (relative risk=0.96; 95% confidence interval=0.41 to 2.26; p=0.930). There was a trend towards a greater hospital mortality rate among patients in the NPPV group (25%) compared to patients in the conventional medical therapy group (0.0%) (p=0.123). Among patients who subsequently required mechanical ventilation, those in the NPPV group had a longer time interval from ED arrival to the start of mechanical ventilation compared to patients in the conventional medical therapy group (26.0±27.0 h vs 4.8±6.9 h; p=0.055).

Conclusions: We conclude that the application of NPPV in the ED may delay tracheal intubation and the initiation of mechanical ventilation in some patients with acute respiratory distress. We also demonstrated that the application of NPPV was associated with an increased hospital mortality rate. Based on these preliminary observations, larger clinical investigations are required to determine if adverse patient outcomes can be attributed to the early application of NPPV in the ED. Additionally, improved patient selection criteria for the optimal administration of NPPV in the ED need to be developed.

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Key words: acute respiratory failure; critical care; mechanical ventilation; noninvasive positive pressure ventilation; outcomes

Abbreviations: APACHE=acute physiology and chronic health evaluation; CI=confidence interval; ED=emergency department; EPAP=expiratory positive airway pressure; IPAP=inspiratory positive airway pressure; NPPV=noninvasive positive pressure ventilation; SaO₂=arterial saturation oxygen

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The management of acute respiratory distress is common in the emergency department (ED) setting. Traditionally, endotracheal intubation and mechanical ventilation have been employed in patients with acute respiratory distress who are unable to meet their ventilatory requirements. However, this form of medical management can be associated with various adverse outcomes, including infectious (eg, nosocomial pneumonia, sinusitis) and noninfectious (eg, barotrauma, oral or laryngeal trauma,
respiratory muscle weakness) complications.1-4 Non-invasive positive pressure ventilation (NPPV) has been used as an alternative method of providing ventilatory support to patients with respiratory failure in order to avoid these complications and to decrease medical care costs.5,6 Several prospective clinical trials have demonstrated the benefits of NPPV for patients with specific disease processes including COPD, cardiogenic pulmonary edema, and asthma.6,10 However, due to the selection of specific subgroups of patients with acute respiratory distress in these investigations, their results may not be applicable to the general patient population evaluated in many EDs.

We conducted a single-center, prospective, randomized clinical trial to determine the effectiveness of NPPV for the treatment of acute respiratory distress in patients presenting to the ED. Additionally, we wished to compare the relative utilization of respiratory care practitioners among patients receiving NPPV and patients receiving conventional medical therapy.

**Materials and Methods**

**Study Location and Patients**

The study was conducted in an urban university-affiliated teaching hospital, Barnes-Jewish Hospital (900 beds). During a 6-month period (July 1996 to December 1996), patients with acute respiratory distress in the ED were potentially eligible for this investigation. Patients were entered into the study if they were older than 18 years and had evidence of acute respiratory distress as demonstrated by the acute onset of moderate to severe dyspnea as assessed by the ED attending physician; a respiratory rate greater than 25 breaths per minute; and one of the following: pH < 7.35, PaCO2 > 45 mm Hg, PaO2 < 55 mm Hg (on room air), arterial saturation oxygen (SaO2) < 90% (on room air), or an alveolar-arterial oxygen pressure difference gradient > 100 mm Hg while receiving supplemental oxygen. Patients were excluded from this investigation if they had any of the following: (1) an immediate indication for endotracheal intubation; (2) hypotension defined as a systolic BP less than or equal to 90 mm Hg despite a 500-mL fluid bolus; (3) presence of a ventricular or atrial arrhythmia; (4) upper airway obstruction or facial trauma; (5) inability to clear secretions from the airway; (6) inability to cooperate with the fitting and wearing of a face mask; (7) presence of a tracheostomy; (8) a predetermined wish not to be intubated or receive mechanical ventilation; (9) an acute exacerbation of asthma; and (10) the presence of a pneumothorax or chest wall trauma. This study was approved by the Washington University School of Medicine Human Studies Committee and informed consent was obtained from all study participants.

**Study Design**

Patients with acute respiratory distress presenting to the ED were randomly assigned to receive conventional medical therapy plus NPPV or to receive conventional medical therapy alone. Randomization was performed using opaque, sealed envelopes which were opened at the time each patient was enrolled in the study. For purposes of this investigation, conventional medical therapy for acute respiratory distress was defined as the administration of supplemental oxygen (titrated by pulse oximetry to keep the SaO2 greater than 90%) and pharmacologic therapy, appropriate for the patient's medical condition, as dictated by the ED and internal medicine attending physicians. Medications used to treat acute respiratory distress included, but were not limited to, inhaled bronchodilators, systemic corticosteroids, intravenous aminophylline, antibiotics, diuretics, vasodilators, inotropes, vasopressors, and electrolyte solutions.

**NPPV Protocol**

Patients randomized to receive NPPV were evaluated by a respiratory care practitioner (ie, a registered respiratory therapist) within 20 min of arrival at the ED. NPPV was delivered by one of two hospital-grade ventilatory support systems (BiPAP, Respironics, Inc; Murrysville, Pa) stationed in the ED. The BiPAP machine is a pressure-limited ventilator that cycles between adjustable inspiratory and expiratory pressures using either patient airflow-triggered or time-triggered cycling modes. NPPV was applied in all patients using a backup respiratory rate of 12 breaths per minute with an initial inspiratory positive airway pressure (IPAP) setting of 8 cm H2O and an initial expiratory positive airway pressure (EPAP) setting of 2 to 4 cm H2O. Respiratory care practitioners assigned to the ED and the medical hospital floors, including the medical intensive care unit, could adjust the levels of IPAP and EPAP according to the ventilatory and gas exchange parameters of the patients. All adjustments in these pressure settings were made by the respiratory care practitioners, according to a NPPV protocol developed at Barnes-Jewish Hospital (see Appendix), after consulting with the attending physician caring for the patient in the appropriate treatment area. Additionally, respiratory care practitioners could administer supplemental oxygen via the BiPAP machine in order to maintain the SaO2 above 90%. A soft cushioned nasal mask (Disposable Nasal Mask, Respironics) was used to provide NPPV. For patients breathing through their mouth, the same mask was employed along with a chin strap to reduce the degree of mouth breathing. Patients requiring emptying of the stomach had an orogastric tube placed to avoid leakage through the mask.

NPPV was begun in the ED and continued on a medical floor or the medical ICU after patient transport from the ED. An adjustable power source for the BiPAP machines allowed their continuous application during patient transports using a 40 amp-h deep-cycle marine type battery. NPPV was maintained until the patient’s respiratory distress resolved, according to clinical criteria and arterial-blood gas findings as determined by the patient’s attending physician, or until the patient required endotracheal intubation and mechanical ventilation.

**Criteria for Intubation**

In order to have a uniform approach to the application of endotracheal intubation, we adopted the criteria developed by Brochard and coworkers. After study enrollment and randomization, intubation was to be performed if any of the following were present: respiratory arrest, respiratory pauses with loss of consciousness or gasping for air; psychomotor agitation making nursing care impossible and requiring sedation; a heart rate below 50 beats per minute with loss of alertness; or hemodynamic instability, defined as a systolic BP below 70 mm Hg. The presence of any of these major criteria was taken as an indication for endotracheal intubation and the initiation of mechanical ventilation.
ventilation. Additionally, respiratory rate and arterial blood gas findings were evaluated as adjunctive criteria for assessing the need for endotracheal intubation. A respiratory rate greater than 35 breaths per minute, an arterial pH below 7.30, and a PaO₂ below 45 mm Hg despite supplemental oxygen therapy were considered supportive of the need for tracheal intubation and mechanical ventilation.

Outcome Measures

The main outcome measure evaluated was the need for endotracheal intubation and mechanical ventilation. We also assessed hospital mortality, admission to the ICU, the length of hospital stay, the duration of mechanical ventilation, the number of acquired organ system derangements using the Organ System Failure Index, and the utilization of respiratory care practitioners providing supportive services to the study patients.

Physiologic Measurements

Systolic and diastolic BP, heart rate, and respiratory rate were measured upon admission to the ED and at 1 h and 24 h after entry into the study. The arterial pH, PaO₂, and PaCO₂ were measured upon arrival to the ED and at 1 h after entry into the study. Additional arterial blood gases were obtained at the discretion of the patients’ attending physicians. The degree of encephalopathy was assessed using a standardized scale where 0 indicated no abnormality in mental status; 1, mild asterixis or tremor; 2, marked asterixis, mild intermittent confusion, or sleepiness during the day; 3, continuous confusion or agitation; and 4, obtundation or major agitation requiring physical or chemical restraints.

Definitions

All definitions were selected prospectively as part of the original study design. The Premorbid Lifestyle score was used as previously defined. A score of 0 indicated that the patient was employed without restriction; 1 indicated that the patient was independent, fully ambulatory, not employed, or employed with restriction; 2 indicated that the patient had restricted activities, could live alone and get out of the house to do basic necessities, or had severely limited exercise ability; 3 indicated that the patient was housebound, could not get out of the house unassisted, could not live alone, or could not do heavy chores; and 4 indicated that the patient was bed- or chair-bound. We calculated APACHE II (acute physiology and chronic health evaluation) scores, and the associated predicted hospital mortality, based on clinical data available from the patient’s stay in the emergency department.

The Organ System Failure Index was modified from that used by Rubin and coworkers. One point was given for acquired dysfunction of each organ system. Renal dysfunction was defined as a twofold increase in baseline creatinine level or an absolute increase in baseline creatinine level of 1.76 mg/dL (150 μmol/L). Hepatic dysfunction was defined as an increase in total bilirubin level to more than 34.2 μmol/L (2.0 mg/dL). Pulmonary dysfunction was defined as (1) a requirement for mechanical ventilation for a diagnosis of pneumonia, COPD, asthma, or pulmonary edema (cardiogenic or noncardiogenic); (2) a PaO₂ of less than 60 mm Hg while receiving a fraction of inspired oxygen of 0.50 or more; or (3) the use of at least 10 cm H₂O of positive end-expiratory pressure. Hematologic dysfunction was defined as the presence of disseminated intravascular coagulation, a leukocyte count of less than 1,000 cells/mm³ (1.0×10⁹/L), or a platelet count of less than 75×10⁹/mm³ (75×10⁹/L). Neurologic dysfunction was defined as a new focal deficit (such as hemiparesis after cerebral infarction) or a new generalized process (e.g., seizures or coma). GI dysfunction was defined as GI hemorrhage requiring transfusion, new ulcers, or diarrhea lasting more than 24 hours and unrelated to previous bowel surgery. Cardiac dysfunction was defined as acute myocardial infarction, cardiac arrest, or the new onset of congestive heart failure.

For purposes of this investigation, the utilization of respiratory care practitioners was defined according to their self-reported activity. A hand-held co- lored monitor (CliniVision; Clinical Information Systems; Ni., Cal.) used to track the daily activity of all respiratory care practitioners at Barnes-Jewish Hospital. The specific respiratory care functions performed (e.g., adjustment of NPPV settings, administration of bronchodilators) along with the duration (in minutes) of services provided to the patient were recorded. This monitoring system is routinely used to develop reports for all charges from the Department of Respiratory Care Services at Barnes-Jewish Hospital.

Statistical Analysis

On the basis of calculations of statistical power, a sample size of 30 patients would allow us to detect, with a 95% probability and a power of 80%, a difference between a postulated 70% rate of endotracheal intubation in patients treated with conventional medical therapy and a 30% rate of endotracheal intubation in patients receiving NPPV.

All comparisons were unpaired and all tests of significance were two-tailed. Continuous variables were compared using Student’s t test or analysis of variance for normally distributed variables and the Wilcoxon rank-sum test for nonnormally distributed variables. The χ² or Fisher’s exact test were used to compare categorical variables. The primary data analysis compared the need for tracheal intubation and mechanical ventilation in patients assigned to receive conventional medical therapy alone and in patients assigned to receive conventional medical therapy plus NPPV. All values are expressed as the mean±SD (continuous variables) or as a percentage of the group from which they were derived (categorical variables). A p value ≤0.05 was considered statistically significant.

Results

Patients

Of the 87 patients evaluated in the ED for acute respiratory distress during the study period, 27 (31.0%) were enrolled into the study. Of the remaining 60 patients not enrolled in this investigation, 34 (56.7%) required emergent tracheal intubation in the ED, 2 (3.3%) had a tracheostomy, 11 (18.3%) had asthma, and 13 (21.7%) were not enrolled due to human error. Sixteen (59.3%) of the study patients were randomized to receive conventional medical therapy plus NPPV, and 11 (40.7%) patients were randomized to receive conventional medical therapy alone. The mean age of the patients was 58.7±11.3 years (range, 39 to 77 years). Sixteen patients (59.3%) were men and 11 (40.7%) were women. The mean APACHE II score of the entire study cohort was 17.1±6.4 (range, 6 to 31) with an average predicted hospital mortality rate of 23.5±13.6%. 
(range, 4.4 to 53.9%). At the time of randomization, no statistically significant differences were found between the two treatment groups for age, gender, ethnicity. Premorbid Lifestyle scores, APACHE II scores or the probability of hospital mortality, history of previous intubation, admission diagnoses, vital signs initially obtained in the ED, encephalopathy score, or arterial blood gas findings (Tables 1, 2).

**Clinical Outcomes and Complications**

Seven patients (43.8%) in the group receiving conventional medical therapy plus NPPV required endotracheal intubation and mechanical ventilation, as compared with 5 patients (45.5%) in the group receiving conventional medical therapy alone (relative risk=0.96; 95% confidence interval [CI]=0.41 to 2.26; p=0.930) (Table 3). The time interval from arrival to the ED until endotracheal intubation was greater for the patients requiring mechanical ventilation who were randomized to receive NPPV compared with those who received conventional medical therapy alone (26.0±27.0 h vs 4.8±6.9 h; p=0.055). The number of acquired organ system derangements during the hospitalization was also greater for patients who received NPPV. No significant differences in nursing home placement, requirement for vasopressors, admission to the ICU, hospital or ICU lengths of stay, or the duration of mechanical ventilation were found between the two study groups. Similarly, no significant differences between the groups in the occurrence of complications during hospitalization were demonstrated (Table 4). One patient in the group randomized to receive conventional medical therapy, who required subsequent endotracheal intubation, developed a lip ulceration secondary to pressure necrosis from the endotracheal tube. None of the patients receiving NPPV developed facial necrosis.

In both treatment groups, a significant improvement was noted in the respiratory rate and heart rate

| Table 2—Vital Signs, Encephalopathy Score, and Arterial Blood Gas Results |
|-------------|-------------|-------------|-------------|-------------|
| Variable    | Patients Receiving NPPV (n=16) | Patients Not Receiving NPPV (n=11) | p Value |
| Heart rate, beats/min | Baseline | 1 h | 24 h | p Value | Baseline | 1 h | 24 h | p Value |
| Mean arterial blood pressure, mm Hg | 109±23 | 95±19 | 93±16 | 0.051 | 116±21 | 112±19 | 94±16 | 0.040 |
| Respiratory rate, breaths/min | 34.4±6.4 | 25±6.4 | 20.9±4.7 | <0.001 | 29.7±6.3 | 24.4±5.6 | 18.0±5.5 | 0.002 |
| Encephalopathy score | 0.4±0.9 | 0.3±0.9 | 0.4±0.8 | 0.987 | 1.2±1.3 | 1.1±1.4 | 0.4±0.8 | 0.406 |
| PaO₂, mm Hg | 50.5±22.3 | 49.3±19.6 | 56.3±26.5 | 0.338 | 56.3±26.5 | 53.3±17.6 | 0.779 |
| Arterial blood pH | 7.34±0.08 | 7.42±0.06 | 7.34±0.09 | 0.031 | 7.34±0.09 | 7.30±0.12 | 0.318 |

p>0.05 for all baseline comparisons between patients receiving NPPV and patients not receiving NPPV.
after initial evaluation in the ED (Table 2). There was also a significant decrease in the mean BP and a significant increase in the arterial pH compared to baseline among patients receiving NPPV. No other significant differences in vital signs, encephalopathy scores, or arterial blood gas findings were demonstrated in the two treatment groups (Table 2).

There was a trend favoring a greater hospital mortality rate among patients receiving NPPV compared with patients receiving conventional medical therapy (25.0% vs 0.0%; p=0.123). The ratio of the actual to predicted mortality rates was greater in the patients receiving NPPV than in the patients receiving conventional medical therapy alone (0.95 vs 0.00). The causes of death in the NPPV group were multiple organ failure (two patients), ARDS (one patient), and nosocomial pneumonia with sepsis (one patient). Hospital nonsurvivors (n=4) had significantly more acquired organ system derangements than hospital survivors did (2.8±1.5 organs vs 1.2±1.0 organs; p=0.011). Similarly, among the 12 patients requiring tracheal intubation and mechanical ventilation, those who experienced more than a 1-hour time interval between arrival at the ED and tracheal intubation (n=9) acquired more organ system derangements than did patients with a shorter interval (n=3) (2.3±1.2 organ systems versus 1.5±0.7 organ systems). However, this difference was not statistically significant (p=0.389).

The average utilization of respiratory care practitioners for the two study groups is shown in Table 5. On day 1, there was a trend towards a greater utilization of respiratory care services among patients receiving NPPV. However, for the remaining individual 4 days examined, and for the total of the first 5 days of hospitalization, no significant differences in the utilization of respiratory care practitioners could be demonstrated between the study groups.

### Table 3—Patient Outcomes During Hospitalization

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients Receiving NPPV (n=16)</th>
<th>Patients Not Receiving NPPV (n=11)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality, no. (%)</td>
<td>4 (25.0)</td>
<td>0 (0.0)</td>
<td>0.123</td>
</tr>
<tr>
<td>Mean no. of acquired organ system derangements per patient</td>
<td>1.8±1.3</td>
<td>0.9±0.7</td>
<td>0.034</td>
</tr>
<tr>
<td>Pulmonary, no. (%)</td>
<td>12 (75.0)</td>
<td>6 (54.5)</td>
<td>0.411</td>
</tr>
<tr>
<td>Cardiac, no. (%)</td>
<td>3 (18.8)</td>
<td>1 (9.1)</td>
<td>0.624</td>
</tr>
<tr>
<td>Renal, no. (%)</td>
<td>5 (31.3)</td>
<td>2 (18.2)</td>
<td>0.662</td>
</tr>
<tr>
<td>Hepatic, no. (%)</td>
<td>2 (12.5)</td>
<td>0 (0.0)</td>
<td>0.499</td>
</tr>
<tr>
<td>Hematologic, no. (%)</td>
<td>5 (31.3)</td>
<td>1 (9.1)</td>
<td>0.350</td>
</tr>
<tr>
<td>Neurologic, no. (%)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Gastrointestinal, no. (%)</td>
<td>1 (6.3)</td>
<td>1 (9.1)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Nursing home placement, no. (%)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Requiring vasopressors, no. (%)</td>
<td>4 (25.0)</td>
<td>2 (18.2)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Length of hospital stay, d</td>
<td>17.4±34.3</td>
<td>9.1±5.7</td>
<td>0.941</td>
</tr>
<tr>
<td>Requiring ICU admission, no. (%)</td>
<td>13 (81.3)</td>
<td>7 (63.6)</td>
<td>0.391</td>
</tr>
<tr>
<td>Length of ICU stay, d</td>
<td>5.8±5.5</td>
<td>4.9±3.2</td>
<td>0.694</td>
</tr>
<tr>
<td>Requiring mechanical ventilation, no. (%)</td>
<td>7 (43.8)</td>
<td>5 (45.5)</td>
<td>0.710</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, no. (%)</td>
<td>5.9±5.2</td>
<td>3.6±2.7</td>
<td>0.393</td>
</tr>
<tr>
<td>Time interval from arrival to ED until endotracheal intubation, h</td>
<td>26.0±27.0</td>
<td>4.8±6.9</td>
<td>0.055</td>
</tr>
</tbody>
</table>

### Table 4—Complications Occurring During the Hospitalization

<table>
<thead>
<tr>
<th>Complication</th>
<th>Patients Receiving NPPV (n=16)</th>
<th>Patients Not Receiving NPPV (n=11)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis, no. (%)</td>
<td>3 (18.8)</td>
<td>1 (9.1)</td>
<td>0.624</td>
</tr>
<tr>
<td>Ileus, no. (%)</td>
<td>2 (12.5)</td>
<td>0 (0.0)</td>
<td>0.499</td>
</tr>
<tr>
<td>Nosocomial pneumonia, no. (%)</td>
<td>0 (0.0)</td>
<td>2 (18.2)</td>
<td>0.157</td>
</tr>
<tr>
<td>Myocardial infarction, no. (%)</td>
<td>2 (12.5)</td>
<td>1 (9.1)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Pneumothorax, no. (%)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Pulmonary embolism, no. (%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Failure to wean, no. (%)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Cardiac arrest, no. (%)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Facial necrosis, no. (%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Oral necrosis, no. (%)</td>
<td>0 (0.0)</td>
<td>1 (9.1)</td>
<td>0.407</td>
</tr>
</tbody>
</table>
DISCUSSION

This preliminary study demonstrated no difference in the need for endotracheal intubation and mechanical ventilation among patients with acute respiratory distress in the ED receiving conventional medical therapy alone vs conventional medical therapy plus NPPV. However, we unexpectedly found a troubling trend towards increased hospital mortality among patients receiving NPPV (25.0% vs 0.0% in patients receiving conventional medical therapy alone). Our study also demonstrated no significant differences between the two study groups in the need for ICU admission, the hospital and ICU lengths of stay, the duration of mechanical ventilation, and the utilization of respiratory care practitioners. This investigation is unique in suggesting the occurrence of a possible detrimental outcome in some patients associated with the early application of NPPV in the ED.

A recent review of NPPV attempted to determine if the available medical literature supported the routine use of this medical technology in patients with acute respiratory failure.14 Four randomized clinical trials examining the application of NPPV for acute respiratory failure were identified,7,9,15,16 These investigations primarily examined patients with COPD, except for the study by Wysocki et al,16 and found either no significant influence of NPPV on hospital mortality or a beneficial effect from its use.7,9,15,16 Only the study by Brochard and colleagues7 demonstrated that the in-hospital mortality rate was significantly reduced among patients receiving NPPV compared to conventional medical therapy (4 of 43 patients [9.3%] vs 12 of 42 patients [28.6%]; p=0.02). The other three studies identified improvements in vital signs, symptom scores, arterial blood gases, and the need for endotracheal intubation with the use of NPPV.9,15,16 Similarly, a number of other uncontrolled studies have reported benefits from the application of NPPV in patients with acute respiratory failure.6,8,10,17-25 However, at the present time there is not a general consensus regarding the routine application of NPPV for acute respiratory failure.26 This is primarily due to the lack of large, prospective, multicenter randomized clinical trials aimed at rigorously determining the efficacy of NPPV in this clinical setting.

Our study results differ from the earlier randomized clinical trials primarily by demonstrating a greater mortality rate among patients receiving NPPV. Our findings also suggest a potential explanation for the increased mortality rate we observed in the NPPV group. Patients receiving NPPV had a longer time interval between ED arrival and the initiation of endotracheal intubation and mechanical ventilation compared with patients in the conventional medical therapy group. This suggests that a delay in the application of endotracheal intubation and mechanical ventilation may have occurred in some patients receiving NPPV, thereby contributing to their worse outcomes. The previous trials of NPPV reported similar timing for endotracheal intubation and the start of mechanical ventilation in different treatment groups.7,16 Delaying the initiation of endotracheal intubation and mechanical ventilation could allow physiologic deterioration of diaphragmatic and lung function to occur, increase the risk of aspiration and nosocomial pneumonia, or delay the onset of other benefits associated with endotracheal intubation and mechanical ventilation in patients with acute respiratory failure (eg, enhanced cardiac function, decreased systemic acidosis, improved mental status).27 Two of our study patients who died had evidence of aspiration and difficulty controlling their secretions during the administration of NPPV, which may have contributed to their poor outcomes.

Several limitations of this preliminary study should be noted. First, we examined a relatively small number of patients, increasing the likelihood for both type I and II statistical errors. Second, we cannot exclude the possibility that bias contributed to our findings. Predetermined biases in favor of the use of NPPV, on the part of the treating physicians or
respiratory care practitioners, may have contributed to the delay in endotracheal intubation we observed among patients receiving NPPV. However, the guidelines we employed for the initiation of endotracheal intubation were designed to minimize such treatment biases. Additionally, the logistical problem of assessing patients for encephalopathy, agitation, and loss of alertness while they wore nasal masks may have contributed to a delay in the clinical recognition of the need for intubation. Third, we did not dictate how conventional medical therapy was to be administered. Therefore, it is possible that differences in medical therapy other than the use of NPPV may have contributed to the observed mortality differences between our study groups. Finally, we did not directly monitor respiratory muscle function. Perhaps more sophisticated monitoring of respiratory muscle function would have allowed us to better determine the lack of efficacy of NPPV, and the need for tracheal intubation.28,29

In summary, we found a significant delay in the application of endotracheal intubation and mechanical ventilation among patients receiving NPPV in the ED for acute respiratory distress. Additionally, patients treated with NPPV had a greater mortality rate than patients receiving conventional medical therapy alone. These findings support the hypothesis that patient selection criteria are critical to the success of NPPV.28 Based on our experience, we agree that a large, well-controlled, multicenter study of NPPV in acute respiratory failure should be performed.14 Such a trial should have three goals. First, it should be designed to clearly establish the efficacy of NPPV in patients with acute respiratory failure evaluated in the ED. Second, it should define the subgroups of patients who are most likely to benefit from the application of NPPV. Third, the optimal ventilatory mode and technical administration of NPPV should be clarified.14,28 Only after such a comprehensive trial is performed can we expect to advance our understanding of the benefits and potential limitations of NPPV. Until that time, clinicians must use the available medical evidence, as well as their own clinical judgment, in deciding which patients with acute respiratory distress should receive NPPV and how long it should be administered prior to endotracheal intubation and mechanical ventilation.

APPENDIX

Protocol for Noninvasive Positive Pressure Ventilation

1. NPPV is implemented per physician order.
2. Obtain a baseline arterial blood gas reading and set up pulse oximetry.
3. Initial NPPV settings
   A. IPAP, 8 cm H2O
   B. EPAP, 2 to 4 cm H2O
   C. Use spontaneous-timed mode with programmed back-up respiratory rate of 12 breaths per minute
   D. Oxygen bleed-in is adjusted to maintain SaO2>92% or per physician-targeted saturation.
4. Explain the procedure to patient, emphasizing breathing in and out through nose. (If patient has difficulty keeping mouth closed, use chin strap.)
5. Assemble the mask, swivel adapter, headgear, and patient circuit or ventilator tubing.
6. Apply mask over patient’s nose, achieving a seal sufficient to prevent any large air leaks around mask.
7. Tighten straps of headgear sufficiently to hold mask in place without large air leaks.
8. Verify that patient is able to nose breathe with reasonable comfort.
9. Adjust IPAP level to provide an adequate tidal volume (8 to 10 mL/kg), decreased respiratory rate, and optimal patient comfort.
10. Adjust the FiO2 and EPAP levels in tandem to maintain SaO2>92% or physician-targeted saturation with lowest FiO2 possible and EPAP <10 cm H2O.
11. Obtain arterial blood gas one hour after initiation of NPPV and as needed according to the patient’s medical condition.
12. Set pressure alarms ±2 cm H2O around the IPAP level.
13. Respiratory care practitioners evaluate patient tolerance of and clinical benefit from NPPV, making all necessary adjustments to assure maximal patient benefit. The respiratory care practitioner must remain in close communication with the patient’s attending physician regarding the physician’s assessment of the patient’s respiratory condition and tolerance of NPPV. Any deterioration in the patient’s clinical parameters (eg, arterial oxygen desaturatation, changing vital signs) will be reported immediately to the patient’s attending physician.

REFERENCES

14 Jasmer RM, Luce JM, Matthay MA. Noninvasive positive pressure ventilation for acute respiratory failure: underutilized or overrated? Chest 1997; 111:1672-78
26 Rosenberg JJ, Goldstein RS. Noninvasive positive pressure ventilation: a positive view in need of supportive evidence. Chest 1997; 111:1479-82