Noninvasive Positive Pressure Ventilation Via Face Mask*

First-Line Intervention in Patients With Acute Hypercapnic and Hypoxemic Respiratory Failure

G. Umberto Meduri, MD, FCCP; Robert E. Turner, RRT; Nabil Abou-Shala, MD, FCCP; Richard Wunderink, MD, FCCP; and Elizabeth Tolley, PhD

Objectives: We have previously reported our experience with noninvasive positive pressure ventilation (NPPV) via face mask in a small group of selected patients with acute respiratory failure (ARF). NPPV was frequently effective (70% success rate) in correcting gas exchange abnormalities and in avoiding endotracheal intubation (ETI); NPPV also had a low rate of complications. We have evaluated the clinical application of NPPV as first-line intervention in patients with hypercapnic and short-term hypoxemic ARF. A dedicated respiratory therapist conducted an educational program with physicians-in-training rotating through the medical ICUs of a university medical center and supervised implementation of a simplified management protocol. Over 24 months, 164 patients with heterogeneous forms of ARF received NPPV. We report on the effectiveness of NPPV in correcting gas exchange abnormalities, in avoiding ETI, and associated complications, in different conditions precipitating ARF.

Patient population: One hundred fifty-eight patients completed the study. Forty-one had hypoxemic ARF, 52 had hypercapnic ARF, 22 had hypercapnic acute respiratory insufficiency (ARI), 17 had other forms of ARF, and 26 with advanced illness had ARF and refused intubation. Twenty-five percent of the patients developed ARF after extubation.

Intervention: Mechanical ventilation was delivered via a face mask. Initial ventilatory settings were continuous positive airway pressure (CPAP) mode, 5 cm H2O, with pressure support ventilation of 10 to 20 cm H2O titrated to achieve a respiratory rate less than 25 breaths/min and an exhaled tidal volume of 7 ml/kg or more. Ventilator settings were adjusted following arterial blood gases (ABG) results.

Results: The mean duration of NPPV was 25±24 h. When the 26 patients with advanced illness are excluded, NPPV was effective in improving or correcting gas exchange abnormalities in 105 patients (80%) and avoiding ETI in 86 (65%). Failure to improve ABG values was the reason for ETI in 20 of 46 (43%). The overall average predicted and actual mortality were 32% and 16%, respectively. Survival was 93% in nonintubated patients and 79% in intubated patients. NPPV was effective in lessening dyspnea throughout treatment in all but seven patients. Complications developed in 24 patients (16%). In patients with hypercapnic ARF, nonresponders had a higher PaCO2 at entrance (91.5±4.2 vs 80±1.5; p<0.01). In patients with hypercapnic ARF and ARI, arterial blood gases response (pH and PaCO2) within 2 h of NPPV predicted success (p<0.0001). None of the entrance parameters predicted need for ETI.

Conclusions: We conclude that application of NPPV in clinical practice is an effective and safe alternative to ETI in many hemodynamically stable patients with hypercapnic ARF and in those with hypoxemic ARF in whom the clinical condition can be readily reversed in 48 to 72 h. An educational and supervision program is essential to successfully implement this form of therapy.

(CHEST 1996; 109:179-93)

ABG=arterial blood gas; APACHE=acute physiology and chronic health evaluation; ARF=acute respiratory failure; CAP=community-acquired pneumonia; CPAP=continuous positive airway pressure; ET=endotracheal tube; ETI=endotracheal intubation; FIO2=fraction of inspired oxygen; FSN=facial skin necrosis; HR=heart rate; MV=mechanical ventilation; NPPV=noninvasive positive pressure ventilation; OAD=obstructive airways disease; PEEP=positive end-expiratory pressure; PEEPf=Intrinsic positive end-expiratory pressure; PSV=Pressure support ventilation; RF=respiratory failure; RR=respiratory rate; RT=respiratory therapist; SIMV=synchronous intermittent mandatory ventilation; VE=minute ventilation; Vr=tidal volume

Key words: asthma; chronic obstructive pulmonary disease; dyspnea, outcome; hypercapnia; hypoxemia; intensive care unit; intermittent positive pressure ventilation; mechanical ventilation; noninvasive ventilation; respiratory insufficiency

*From the Department of Medicine, Pulmonary and Critical Care Division (DrS. Meduri, Abou-Shala, and Wunderink, and Mr. Turner), and Department of Preventive Medicine, Division of Biostatistics and Epidemiology (Dr. Tolley), the University of Tennessee Medical Center, Regional Medical Center, and Veteran Affairs Medical Center, Memphis. Supported in part by Puritan-Bennett Grant R07-3340-67. Manuscript received April 13, 1995; revision accepted August 22. Reprint requests: Dr. Meduri, The University of Tennessee, Memphis, 956 Court Avenue, Room H314, Memphis, TN 38163
Acute respiratory failure (ARF) refers to a severe deterioration in gas exchange that may require mechanical ventilation (MV) for life support. Instituted when conservative treatment fails, MV aims to correct gas exchange abnormalities and to rest the respiratory muscles, while concomitant interventions are directed at correcting the underlying condition that resulted in ARF. Traditionally, an endotracheal tube (ET) is inserted to deliver the mechanical tidal breath to the patient’s lungs. Placing this artificial airway is invasive and associated with discomfort and potential complications. Although the need for endotracheal intubation (ETI) is undisputed for long-term support of patients with ARF, discrimination of which patients with ARF will require prolonged MV is often difficult.1

Following the encouraging results of a small pilot study,2 we investigated using noninvasive positive pressure ventilation (NPPV) in patients with hypercapnic respiratory failure (RF) and in patients with advanced illness who developed RF and refused intubation.1,3 Our results agree with the experience of other groups,4–32 indicating that NPPV is effective in correcting gas exchange abnormalities in most patients with ARF and avoids the need for intubation in 70%. Furthermore, NPPV was associated with a low rate of complications and a decreased duration of MV and ICU stay. Therefore, we conducted a large prospective study to evaluate the clinical application of NPPV as first-line intervention in patients with hypercapnic and short-term hypoxemic ARF. In 1992, a systematic educational program was instituted by a dedicated respiratory therapist (RT) who supervised implementing a simplified treatment protocol at two medical ICUs. We report our experience on 164 consecutive patients with heterogenous forms of ARF and in whom NPPV was attempted. The purpose of the study was to characterize the response to NPPV in different clinical setting(s) and to identify predictors of response, reasons and timing of failure, type of complications, and consequences of postponing intubation in nonresponders.

**Materials and Methods**

The study was conducted from March 1992 to March 1994 at the University of Tennessee Health Science Center in Memphis in the medical ICUs of the Regional Medical Center and Veterans Affairs Medical Center. The study was approved by the Institutional Review Board. An educational program was conducted monthly by a dedicated RT for house staff and fellows rotating through these medical ICUs and for ICU nurses and RTs. This program included an instructional videotape to demonstrate methodology of NPPV (available from us on request). The intervention protocol was supervised during the daytime (weekends excluded) by the RT.

The patient population was divided into five groups. Diagnostic criteria for hypoxemic respiratory failure (group 1), hypercapnic respiratory failure (group 2), and hypercapnic respiratory insufficiency (group 3) are shown in Table 1. Patients in respiratory distress not meeting these criteria were defined as others (group 4).

### Table 1—Definitions of ARF*  

<table>
<thead>
<tr>
<th></th>
<th>Hypoxemic</th>
<th>Hypercapnic</th>
<th>Hypercapnic Respiratory Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>Severe</td>
<td>Severe</td>
<td>moderate-severe</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>&gt;30 breaths/min</td>
<td>&gt;25 breaths/min</td>
<td>&gt;25 breaths/min</td>
</tr>
<tr>
<td>pH</td>
<td>—</td>
<td>—</td>
<td>&lt;7.30</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>—</td>
<td>&gt;60</td>
<td>&lt;7.30</td>
</tr>
<tr>
<td>PaO₂/FIO₂</td>
<td>&lt;200</td>
<td>—</td>
<td>&gt;45</td>
</tr>
<tr>
<td>Urgent need for MV</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

*Definitions relied on the presence of all above parameters. Patients without all parameters were classified as others.

The decision that the patient needed urgent application of MV, with intubation if NPPV was not provided, was established on clinical criteria. Patients with advanced disease with urgent need for MV, but who refused ETI, were analyzed separately (group 5). Furthermore, patients were categorized into 13 diagnostic groups based on the condition precipitating respiratory failure (Table 2).

Criteria for excluding patients from the study included the following: (1) systolic BP less than 90 mm Hg or the use of vasopressors; (2) ECG instability with evidence of ischemia or significant ventricular arrhythmias; (3) need for ETI to protect the airways (coma or seizure disorders) or to manage secretions; or (4) life-threatening hypoxemia (O₂ saturation <90%, or PaO₂ <60 mm Hg, on nonbreathing face mask). Criteria for exit from the study included the following: (1) inability to improve gas exchange, dyspnea, or lethargy; (2) development of conditions necessitating ETI; (3) hemodynamic or ECG instability; (4) inability to tolerate the face mask because of discomfort; (5) inability to properly fit the face mask; or (6) patient request.

The method of NPPV is shown in Figure 1. The method was simplified to facilitate implementation outside the research environment. The ventilator was connected with conventional ventilator tubing to a clear, full-face mask (Benefit; Puritan Bennett Co; Overland Park, Kan). The masks used were available in two adult sizes: medium and large. The head of the bed was raised to an angle of 45° or more and kept elevated during NPPV to minimize the risk of aspiration. The mask was gently placed over the patient’s face and kept in position by the RT for a few minutes until the patient was comfortable and in full synchrony with the ventilator (continuous positive airway pressure [CPAP] pressure 0 H₂O, and pressure support ventilation [PSV] 10 H₂O). The face mask was then secured by head straps (Fig 2), avoiding a tight fit. To minimize air leakage, tincture of benzoic was frequently smeared over the mask’s cushion to favor sealing with the skin interface. In most patients, a skin patch (Duodermı; Bristol Myers-Squibb; Princeton, NJ) was applied over the nasal bridge to minimize skin necrosis and at other contact sites to seal air leaks. Nasogastric suction was applied only if the patient’s gastric distention.

All patients received MV from a ventilator (Puritan Bennett 7200; Puritan Bennett Co). The humidifier had water, but the heater was turned off. After the mask was secured, CPAP of 5 cm H₂O was applied and PSV was increased to obtain the largest (>7 mL/kg) exhale tidal volume (Vr), a respiratory rate of less than 25 breaths/min, and patient comfort. If a significant leak around the mask prevented the use of PSV or if the patient had a low respiratory rate, the synchronized intermittent mandatory ventilation (SIMV) mode was used. Ventilation was initially delivered continuously, similar to our previous reports.1,3 After the first 4 to 6 h of
Table 2—Patient Population and Outcome

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>No.</th>
<th>Groups* 1-2-3-4-5</th>
<th>Improved Gas Exchange1 (%)</th>
<th>Required Intubation (%)</th>
<th>Predicted Mortality2 (%)</th>
<th>Actual Mortality2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD with acute exacerbation</td>
<td>51</td>
<td>6-22-8-4-11</td>
<td>39 (78)</td>
<td>9 (18)</td>
<td>28±11%</td>
<td>3 (6)</td>
</tr>
<tr>
<td>COPD with pneumonia</td>
<td>27</td>
<td>6-11-4-2-4</td>
<td>20 (74)</td>
<td>11 (41)</td>
<td>35±21%</td>
<td>2 (7)</td>
</tr>
<tr>
<td>COPD with congestive heart failure</td>
<td>12</td>
<td>1-5-3-0-3</td>
<td>5 (42)</td>
<td>6 (46)</td>
<td>25±16%</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Status asthmatic</td>
<td>5</td>
<td>0-4-1-0-0</td>
<td>5 (100)</td>
<td>1 (20)</td>
<td>8±10%</td>
<td>0</td>
</tr>
<tr>
<td>Acute upper airway obstruction</td>
<td>3</td>
<td>0-0-3-0-0</td>
<td>3 (100)</td>
<td>1 (33)</td>
<td>31±23%</td>
<td>0</td>
</tr>
<tr>
<td>End-stage lung cancer</td>
<td>3</td>
<td>0-0-0-1-2</td>
<td>1 (33)</td>
<td>0 (0)</td>
<td>35±22%</td>
<td>2 (67)</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>5</td>
<td>1-2-1-0-1</td>
<td>5 (100)</td>
<td>1 (20)</td>
<td>45±22%</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Cardiogenic pulmonary edema</td>
<td>9</td>
<td>3-1-1-4-1</td>
<td>8 (89)</td>
<td>4 (44)</td>
<td>52±23%</td>
<td>2 (22)</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>14</td>
<td>7-2-0-2-3</td>
<td>11 (79)</td>
<td>4 (29)</td>
<td>40±23%</td>
<td>5 (36)</td>
</tr>
<tr>
<td>AIDS with opportunistic pneumonia†</td>
<td>11</td>
<td>8-0-1-1-1</td>
<td>8 (73)</td>
<td>2 (18)</td>
<td>29±15%</td>
<td>4 (36)</td>
</tr>
<tr>
<td>ARDS</td>
<td>3</td>
<td>2-0-0-1-0</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>40±17%</td>
<td>1 (33)</td>
</tr>
<tr>
<td>Obesity hypoventilation</td>
<td>3</td>
<td>1-2-0-0-0</td>
<td>2 (67)</td>
<td>0 (0)</td>
<td>14±10%</td>
<td>0</td>
</tr>
<tr>
<td>Others†</td>
<td>12</td>
<td>6-3-1-2-0</td>
<td>10 (83)</td>
<td>5 (42)</td>
<td>37±24%</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Total</td>
<td>158</td>
<td></td>
<td>119 (76)</td>
<td>46 (29)</td>
<td>32±19%</td>
<td>25 (16)</td>
</tr>
</tbody>
</table>

*Definitions of groups: 1=hypoxemic RF; 2=hypercapnic RF; 3=hypercapnic respiratory insufficiency; 4=others; 5=patients with advanced disease who refused intubation.

†Improved gas exchange included patients' significant improvement or correction in ABG values. See text for explanation.

‡There was no statistically significant difference between predicted mortality by the APACHE II score31 and actual mortality.

§Opportunistic pneumonia included nine Pneumocystis carinii pneumonia and two disseminated histoplasmosis.

‖Others included salicylate toxicity (1), toxic gas inhalation (1), pulmonary hemorrhage (1), smoke inhalation (1), chemotherapy-induced lung disease (1), large pleural effusion (2), fluid overload (1), chest trauma (1), and sepsis (3).

Continuous NPPV, patients had periods of "rest" (15 to 30 min) off the mask while receiving supplemental oxygen, fluids, or dietary liquid supplements. The fraction of inspired oxygen (FiO2) was titrated to achieve an oxygen saturation greater than 90%. In patients with hypoxemic respiratory failure, CPAP was increased in increments of 2 to 3 cm H₂O until FiO₂ requirements were 0.6 or less. Ventilator settings were adjusted based on results of arterial blood gases (ABGs) obtained within 2-h, 2- to 6-h, and 6- to 12-h intervals following initiation of NPPV. Patients received continuous ECG and arterial oxygen saturation monitoring. Patients were examined at regular intervals for abdominal distention and for their ability to clear secretions or to protect the airways.

Patients were weaned from MV following improvement in respiratory failure, by removing the ventilator once PSV was 5 cm H₂O or less or by titrating periods off MV to patient tolerance and objective findings, similar to a T-piece weaning trial. Patients then received supplemental oxygen by nasal cannula or face mask. Standard therapy directed toward the etiology of the underlying condition and cause of respiratory failure was maintained during noninvasive ventilation (eg, patients continued to receive bronchodilator therapy, etc).

The following data were collected: age, gender, race, acute physiology and chronic health evaluation (APACHE II) score and predicted mortality;35 type of respiratory failure, condition precipitating respiratory failure, presence of paradoxical abdominal motion, use of accessory muscles of respiration, refusal of intubation in patients with advanced disease, mode of ventilation (PSV vs SIMV), duration of NPPV in hours, reasons to exit the study, reasons to discontinue NPPV, indications for ETI, timing of ETI, complications of NPPV, and survival of ICU admission. Complications of NPPV specifically monitored included local tissue damage (facial skin necrosis), ability to mobilize secretions, development of

![Figure 1. Methodology of noninvasive positive pressure ventilation.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21726/ on 06/01/2017)
Figure 2. Patient receiving noninvasive positive pressure ventilation.

pneumonia by clinical and radiographic criteria, and abdominal
distention.

The following sequential data were recorded at entrance into
the study (baseline) and at 2- to 6-h intervals: (1) subjective
response: dyspnea quantitated by a modified Borg dyspnea score24 (4 to
5=severe; 2 to 3=mild; 0=none), degree of comfort
with NPPV, and mental alertness; (2) objective response:
respiratory rate (RR), BP, and heart rate (HR); and (3) physiologic
response: PaO2:FIO2, pH, minute ventilation (Ve), and exhaled Vt
measured by the ventilator expiratory flow sensor (the total volume
is reduced by the compliance volume measured in the patient
circuit).

ABG response was defined as (1) corrected, (2) improved, or (3)
not improved by comparing entrance ABG (prior to initiating
NPPV) to the best result obtained within 24 h of NPPV. In the hy¬
poxemic group, corrected=PaO2:FIO2 increased by more than 100,
improved=PaO2:FIO2 increased by more than 50; not improved=PaO2:FIO2
increased by less than 50. In the hypercapnic groups,
corrected=increase in pH to 7.35 or more, improved= in¬
crease in pH of 0.1 or more from baseline, not improved=increase
in pH of less than 0.1 from baseline and less than 7.35. The patient
sample was divided into responders (ABG corrected or improved)
and nonresponders (ABG not improved).

Statistical Analysis

We evaluated patients repeatedly at baseline (prior to instituting
NPPV), 1 to 2 h, 2 to 6 h, 6 to 12 h, and 12 to 24 h into NPPV. Re¬
response variables were PaO2:FIO2, PaCO2, pH, RR, HR, and dys¬
pnea score. ABGs were available at baseline in 154 patients, at the
1- to 2-h interval in 122, at the 2- to 6-h interval in 72, at the 6- to
12-h interval in 69, and at the 12- to 24-h interval in 82.

Generally, the following analyses were completed within groups
of patients having similar types of respiratory failure. For variables
not affected by type of failure, the entire patient sample was
included in the analyses. We compared average responses for all
variables at the evaluation times using t tests in the context of re¬
peated measures analyses of variance.35 At the conclusion of
the study, we determined whether those patients whose conditions
improved while using NPPV (ie, responders) differed from patients
whose conditions failed to improve (ie, nonresponders). For these
analyses, we used χ² tests for contingency tables, Fisher’s Exact
Two-tailed Test for 2x2 tables, and Mann-Whitney U tests for
continuous variables. In addition, we compared responders and
nonresponders overall and at each evaluation time using t tests in
the context of analyses of variance for the typical split-plot ex¬
perimental design.

RESULTS

Over the 24-month period of the study, the number of
patients receiving MV with either ETI or NPPV in
the two medical ICUs was 674, an average of 28 per
month. During that interval, NPPV was attempted in
164 patients (24%), including 26 patients who had re¬
fused intubation prior to study entry. NPPV was suc¬
cessful in avoiding intubation in 65% (86/132) of the
patients in which it was attempted and in 13% (86/642)
of all patients receiving MV. Most patients in whom
NPPV was not attempted had received ETI in the
emergency department or ward prior to contact by the
ICU team. The average number of patients attempted
on NPPV increased from 2.2 per month in the first 10
months to 10 per month in the last 14 months. Six pa¬
tients receiving NPPV required intubation for a surgical
procedure and exited the study, despite correction of
gas exchange abnormalities during NPPV. The study
population, therefore, consisted of 158 patients.

Table 3—Demographic and Physiologic Parameters at Initiation of NPPV

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Hypoxemic Failure</th>
<th>Hypercapnic Insufficiency</th>
<th>Others</th>
<th>Refused Intubation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>56±14</td>
<td>62±14</td>
<td>64±16</td>
<td>66±9</td>
<td>61±13</td>
</tr>
<tr>
<td>Female/male</td>
<td>9/32</td>
<td>10±19</td>
<td>6/11</td>
<td>1/25</td>
<td>35/23</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>118±26</td>
<td>117±21</td>
<td>121±17</td>
<td>112±15</td>
<td>114±22</td>
</tr>
<tr>
<td>RR, breaths/min</td>
<td>31±10</td>
<td>31±10</td>
<td>29±10</td>
<td>33±9</td>
<td>30±9</td>
</tr>
<tr>
<td>Dyspnea score†</td>
<td>3±1</td>
<td>3±1</td>
<td>3±1</td>
<td>3±1</td>
<td>3±1</td>
</tr>
<tr>
<td>pH</td>
<td>7.39±0.07</td>
<td>7.32±0.04</td>
<td>7.35±0.1</td>
<td>7.29±0.1</td>
<td>7.31±0.09</td>
</tr>
<tr>
<td>PaCO₂ mm Hg</td>
<td>42±12</td>
<td>61±14</td>
<td>43±12</td>
<td>70±28</td>
<td>63±24</td>
</tr>
<tr>
<td>PaO₂:FIO₂</td>
<td>110±46</td>
<td>249±126</td>
<td>162±77</td>
<td>182±100</td>
<td></td>
</tr>
<tr>
<td>Postextubation RF (%)‡</td>
<td>10±24</td>
<td>6±27</td>
<td>8±47</td>
<td>2±8</td>
<td>39±25</td>
</tr>
<tr>
<td>APACHE II</td>
<td>21±6</td>
<td>17±6</td>
<td>20±6</td>
<td>23±7</td>
<td>20±6</td>
</tr>
</tbody>
</table>

*All parameters are reported as mean±SD.
†Modified Borg dyspnea score: 4 to 5=severe; 2 to 3=mild; 1 to 2=mild; 0=none.
‡Seven patients were status post self-extubation.
Table 4—Ventilatory Requirements at Initiation of NPPV

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Hypoxemic Failure</th>
<th>Hypercapnic Failure</th>
<th>Hypercapnic Insufficiency</th>
<th>Others</th>
<th>Refused Intubation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td>41 (26)</td>
<td>52 (33)</td>
<td>22 (13)</td>
<td>7 (10)</td>
<td>26 (16)</td>
<td>158</td>
</tr>
<tr>
<td>SIMV (%)</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>CPAP, cm H2O</td>
<td>5.1 (5-10)</td>
<td>5.5 (5-10)</td>
<td>5.1 (5-6)</td>
<td>4.6 (3-5)</td>
<td>5 (5-10)</td>
<td>5 (3-10)</td>
</tr>
<tr>
<td>Fio2</td>
<td>0.66 (0.28-1.0)</td>
<td>0.47 (0.24-1.0)</td>
<td>0.41 (0.24-1.0)</td>
<td>0.55 (0.29-1.0)</td>
<td>0.50 (0.26-1.0)</td>
<td>0.54 (0.24-1.0)</td>
</tr>
<tr>
<td>Exhaled Vr, L</td>
<td>0.65 (0.28-1.0)</td>
<td>0.52 (0.35-0.7)</td>
<td>0.64 (0.4-1.3)</td>
<td>0.53 (0.4-0.6)</td>
<td>0.58 (0.3-1.0)</td>
<td>0.60 (0.28-1.3)</td>
</tr>
<tr>
<td>Ve, L</td>
<td>17 (3-28)</td>
<td>11 (3-19)</td>
<td>14 (6-27)</td>
<td>16 (5-23)</td>
<td>15 (6-21)</td>
<td>15 (3-28)</td>
</tr>
</tbody>
</table>

*All parameters are reported as medians because some variables are highly skewed.

1Parameters obtained at initiation of NPPV.

Findings at Entrance and Initial Ventilatory Requirements

Patients included 123 men and 35 women. Patients were divided into five groups: 41 had hypoxemic ARF, 52 had hypercapnic ARF, 22 had hypercapnic acute respiratory insufficiency (ARI), 17 had other forms of ARF, and 26 refused ETI (Table 3). Seventy-four patients were black and 84 were white. Demographics and physiologic parameters at initiation of NPPV for patients in the five groups are shown in Table 3. Conditions precipitating ARF and outcome are shown in Table 2. Ventilatory requirements at initiation of NPPV are shown in Table 4.

Response to NPPV

The overall response to NPPV is shown in Table 5. NPPV was effective in lessening dyspnea throughout treatment in all but seven (4%) patients. The respiratory rate decreased from 30±8 at baseline to 23±9, and 21±8 at the less than 2-h and 6- to 12-h interval, respectively (p<0.0001 from baseline for both measurements). A reduction in RR to less than 25 breaths/ min was achieved in 57% within the first 2 h of treatment. The dyspnea score decreased from 3.1±0.7 at baseline to 2.3±0.8, 2±0.1, and 1.8±0.1 at the less than 2-h, 2- to 6-h, and 6- to 12-h intervals, respectively (p<0.0001 from baseline for both measurements).

ABG response is shown in Table 5. When group 5 is excluded, intubation was required in 46 patients (35%), 58% of nonresponders and 28% of responders (p=0.002). Reasons to discontinue NPPV and to intubate are shown in Table 6. Reasons for intubation over time are shown in Figure 3. Intubation was required in 23 patients within 12 h, and in 15 after 24 h of NPPV. Figure 4 shows the relation between type of ABG response, intubation rate, and outcome. Survival in responders (group 5 excluded) was 89% vs 53% in nonresponders (p=0.5). Among responders, mortality was lower in nonintubated than in intubated patients (7% vs 24%; p=0.04). Among nonresponders, mortality was also lower in nonintubated than in intubated patients (8% vs 21%; p=0.3). The adjusted relative risk of death for those patients who were intubated vs those who were not, after adjusting for ABG response, was 2.99 (95% confidence interval, 1.16 to 7.69; p=0.023). The length of time MV was required in 112 nonintubated patients was less than 2 h in 2, 2 to 6 h in 11, 6 to 12 h in 21, 12 to 24 h in 33, and more than 24 h in 45.

Table 5—Response to NPPV

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypoxemic Failure</th>
<th>Hypercapnic Failure</th>
<th>Hypercapnic Insufficiency</th>
<th>Others</th>
<th>Refused Intubation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td>41 (26)</td>
<td>52 (33)</td>
<td>22 (13)</td>
<td>17 (10)</td>
<td>26 (16)</td>
<td>158</td>
</tr>
<tr>
<td>Duration in hours*</td>
<td>26 (2-192)</td>
<td>22 (1-89)</td>
<td>23 (2-72)</td>
<td>23 (3-57)</td>
<td>31 (4-97)</td>
<td>25 (1-192)</td>
</tr>
<tr>
<td>ABG correction (%)</td>
<td>20 (49)</td>
<td>31 (60)</td>
<td>13 (59)</td>
<td>9 (53)</td>
<td>15 (58)</td>
<td>88 (56)</td>
</tr>
<tr>
<td>ABG improvement (%)</td>
<td>11 (26)</td>
<td>15 (29)</td>
<td>3 (14)</td>
<td>1 (6)</td>
<td>2 (8)</td>
<td>32 (20)</td>
</tr>
<tr>
<td>ABG no improvement (%)</td>
<td>10 (24)</td>
<td>6 (11)</td>
<td>6 (27)</td>
<td>7 (41)</td>
<td>9 (35)</td>
<td>38 (24)</td>
</tr>
<tr>
<td>No. of intubations (%)</td>
<td>14 (34)</td>
<td>15 (29)</td>
<td>10 (45)</td>
<td>7 (41)</td>
<td>NA</td>
<td>46 (35)</td>
</tr>
<tr>
<td>Intubated died (%)</td>
<td>5 (12)</td>
<td>1 (2)</td>
<td>4 (18)</td>
<td>0</td>
<td>NA</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>8 (20)</td>
<td>6 (12)</td>
<td>3 (14)</td>
<td>5 (29)</td>
<td>3 (12)</td>
<td>25 (16)</td>
</tr>
<tr>
<td>Discontinue NPPV (%)</td>
<td>16 (58)</td>
<td>17 (34)</td>
<td>12 (45)</td>
<td>5 (29)</td>
<td>7 (5)</td>
<td>37 (26)</td>
</tr>
<tr>
<td>ICU mortality (%)</td>
<td>9 (22)</td>
<td>1 (2)</td>
<td>4 (18)</td>
<td>2 (12)</td>
<td>9 (35)</td>
<td>25 (16)</td>
</tr>
<tr>
<td>Predicted mortality</td>
<td>0.40±0.19</td>
<td>0.26±0.15</td>
<td>0.22±0.19</td>
<td>0.33±0.17</td>
<td>0.40±0.22</td>
<td>0.32±0.19</td>
</tr>
</tbody>
</table>

*Expressed as median and range (in parentheses).

1Complications included FSN in 20, nosocomial pneumonia in 1 (group 2), auto-PEEP in 1 (group 2), gastric distention in 3 (groups 1, 2, and 3).

1Reasons for discontinuing NPPV are shown in Table 6.

1Predicted mortality by APACHE II score.31
Table 6—Reasons to Discontinue NPPV and Need for Intubation in Responders and Nonresponders*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Responders</th>
<th>Nonresponders</th>
<th>Intubated</th>
<th>Nonintubated</th>
<th>Intubated</th>
<th>Nonintubated</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to correct ABG values</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td>0</td>
<td></td>
<td></td>
<td>20 (38)</td>
</tr>
<tr>
<td>Inability to decrease dyspnea</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td>7 (13)</td>
</tr>
<tr>
<td>Management of secretions</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td>4 (8)</td>
</tr>
<tr>
<td>Intolerance to NPPV</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>6 (10)</td>
</tr>
<tr>
<td>Hemodynamic instability</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
<td>6 (12)</td>
</tr>
<tr>
<td>Poorly fitting mask</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td>3 (6)</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td>6 (12)</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>52</td>
</tr>
</tbody>
</table>

*Five patients from group 5 who had NPPV discontinued (see Table 5) are not included in this Table.

Complications

As shown in Table 5, complications during NPPV occurred in 24 patients (15%): 20 (13%) facial skin necrosis (FSN), 3 (2%) gastric distention requiring insertion of a nasogastric tube, 1 nosocomial pneumonia (also developed FSN), and 1 unilateral lung hyperinflation. FSN healed spontaneously in less than 1 week. Development of FSN was not influenced by duration (in hours) of NPPV (25±24 vs 25±17; p=0.09), age, type of respiratory failure, level of pressure applied (either CPAP or PSV), or serum albumin level. Gastric distention was not related to the use of higher PSV (14±4 vs 20±5; p=0.2) and was not associated with clinical aspiration. Nosocomial pneumonia occurred in one patient 64 h into uncomplicated (no gastric distention) NPPV. The patient required ETI and survived ICU stay. No other serious complications occurred as a result of delaying intubation in patients failing NPPV. One patient with COPD and hypercapnic ARF developed unilateral hyperinflation with worsening oxygen saturation 30 h into successful NPPV; the problem was resolved after removal of NPPV without requiring intubation. The patient was suspected to have unilateral bronchial obstruction from retained secretions and required no further treatment.

Types of Respiratory Failure

Postextubation ARF comprised a large percentage of patients in each group of ARF (Table 3). These pa-
patients (described later) were analyzed separately and found to have a response similar to the one of the other five groups after removal of those with postextubation ARF.

**Hypoxemic Respiratory Failure**: Conditions precipitating hypoxemic ARF are shown in Table 2. Fourteen patients (34%) required intubation (10 responders and 4 nonresponders) for the following reasons: inability to correct gas exchange (7), inability to improve dyspnea (2), management of secretions (2), or others (3). No variable at initiation of NPPV discriminated patients who required intubation. The changes in PaO₂/FiO₂ over time in responders and nonresponders are shown in Figure 5. Two patients required a CPAP level of 8 cm H₂O or more to maintain FiO₂ of less than 0.6. Nine patients died during ICU stay (3 AIDS, 2 community-acquired pneumonia [CAP], 1 COPD exacerbation, 1 ARDS, 1 cardiogenic pulmonary edema, 1 other), and five (intubated) died during treatment of ARF. Mortality rate in patients requiring intubation was 35%. Causes of death in intubated patients included the following: one septic shock and four respiratory failure (two patients with advanced carcinoma, one AIDS, and one COPD). Causes of death in nonintubated patients included one progressive cardiovascular event, cardiac failure in two patients with AIDS, and one cardiac arrest in a do-not-resuscitate patient.

**Hypercapnic Respiratory Failure and Insufficiency**: Seventy-four patients had hypercapnic failure (52) or insufficiency (22). Precipitating conditions are shown in Table 2. Twenty-five patients (34%) required intubation (16 responders and 9 nonresponders) for the following reasons: inability to correct gas exchange (12), inability to improve dyspnea (4), hemodynamic instability (3), intolerance to the mask (2), inability to manage secretions (1), and others (3). Among patients with COPD, intubation rate was higher in those with pneumonia (47%) or congestive heart failure and lower in patients with acute exacerbation of COPD (17%). The changes in PaCO₂ and pH over time in responders and nonresponders with hypercapnic ARF are shown in Figure 6. Five patients died during ICU stay, all of them were intubated (3 COPD, 1 restrictive lung disease, 1 other). Mortality rate in intubated patients was 20%. Two deaths were related to progressive respiratory failure and three to multiple organ dysfunction syndrome.

**Others**: Seventeen patients had ARF without meeting the preset criteria for groups 1 to 3. Conditions precipitating ARF are shown in Table 2. Seven patients (41%) required intubation (four nonresponders) for the following reasons: hemodynamic instability (3).

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**Legend**: Figures 4 and 5.

**Figure 4**: Relationship among type of response, intubation, and survival. NS=nonsurvivors.

**Figure 5**: PaO₂/FiO₂ changes over time in patients with hypoxemic respiratory failure. Responders=labeled triangle with solid line; nonresponders=labeled circles with dashed line.
inability to improve gas exchange (1), inability to improve dyspnea (1), management of secretions (1), and others (1). Complications during NPPV occurred in five (29%) patients: FSN (4), gastric distention (1). Two (12%) patients died during ICU stay (1 cardiogenic pulmonary edema, 1 lung cancer). None of them were intubated at the time of death and death was not related to ARF.

Patients Refusing Intubation: Twenty-six patients with advanced illness developed ARF and expressed the wish not to be intubated (group 5): 18 end-stage COPD with exacerbation, 3 severe CAP (end-stage liver disease, end-stage COPD, lung cancer), 2 lung cancer, 1 AIDS with opportunistic pneumonia, and 2 others. The dyspnea score decreased from 3±0.3 at baseline to 2±0.3 and 1.5±0.4 at the less than 2-h, to 2- to 6-h, and 6- to 12-h intervals, respectively. Nine (35%) patients died during ICU stay (three COPD, three CAP, one AIDS, one lung cancer, and one restrictive lung disease). In five of these patients, NPPV was discontinued at the patient’s or the family’s request after failure to improve.

Conditions Precipitating Respiratory Failure in Groups 1 to 4

Postextubation Respiratory Failure: Thirty-seven patients developed respiratory failure postextubation (self-extubation in seven). Causes of ARF included COPD (17), severe CAP (4), congestive heart failure (5), and others (11). The mean (±SD) age was 62±15 years; 28 were male. Findings prior to instituting NPPV were pH of 7.32±0.01, PaCO2 of 57±17, PaO2:FIO2 of 204±106, RR of 31±9, HR of 112±22, and dyspnea score of 3.6±1.1. Duration of NPPV was 25±22 h. Six (15%) failed to improve gas exchange. Thirteen (35%) required intubation (4 for inability to improve ABG values). Five developed complications.

Patients With COPD: Seventy-two patients with COPD developed respiratory failure or insufficiency (Table 2). The mean (±SD) age was 67±7 years; 59 were male. Findings prior to instituting NPPV were pH of 7.30±0.08, PaCO2 of 70±20, PaO2:FIO2 of 207±112, RR of 27±9, HR of 115±21, and dyspnea score of 3±1.1. Duration of NPPV was 23±17 h. Eighteen (25%) patients failed to improve gas exchange. Twenty-six (36%) required intubation (16 for inability to improve ABG values). Thirteen developed complications. Mortality was 6%. An additional 19 patients with advanced COPD belonged to group 5. NPPV corrected (11) or improved (1) gas exchange in 63%, and mortality rate was 15%.

Patients With Severe CAP: Eleven patients without COPD were admitted to the ICU with severe CAP and respiratory failure or insufficiency (Table 2). Their mean (±SD) age was 59±10 years; eight were male. Findings prior to instituting NPPV were pH of 7.34±0.08, PaCO2 of 45±21, PaO2:FIO2 of 153±123, RR of 30±10, HR of 111±22, and dyspnea score of 3.3±1.3. Duration of NPPV was 28±23 h. Three (27%) patients failed to improve ABG values. Intubation was necessary in four (36%) patients for the following reasons: management of secretions (2), intolerance to the mask (1), and others (1). None developed complications.

When patients with COPD and with advanced disease (group 5) are included, a total of 41 patients with pneumonia entered the study. Intubation was required in 15 (36%) and in only 3 due to inability to clear secretions. Overall predicted and actual mortality were 37% and 17%, respectively. Predicted and actual mortality in group 1 (13 patients) was 40% and 15%; in groups 2 and 3 combined (17 patients), 25% and 6%; in group 4 (4 patients), 47% and 0%; and in group 5 (7 patients), 49% and 57%, respectively.

Patients With AIDS and Opportunistic Pneumonia: Ten patients with AIDS were admitted to the ICU with opportunistic pneumonia and respiratory failure or insufficiency (Table 2). Their mean (±SD) age was 37±9 years; six were male. Findings prior to instituting NPPV were pH of 7.36±0.09, PaCO2 of 38±9, PaO2:FIO2 of 132±71, RR of 37±10, HR of 126±29, and dyspnea score of 4±1. Duration of NPPV was 39±28 h. Two (20%) patients failed to improve ABG.
values and required intubation. One developed complications.

Patients With Status Asthmaticus: Five patients were admitted to the ICU with acute asthmatic attack and respiratory failure or insufficiency. Their mean (±SD) age was 49±23 years; two were male. Findings prior to instituting NPPV were pH of 7.24±0.08, PaCO₂ of 67±13, PaO₂:FIO₂ of 207±93, RR of 29±6, HR of 114±15, and dyspnea score of 3.4±0.5. All patients corrected (4) or improved (1) ABG values. Duration of NPPV was 31±18 h. Intubation was necessary in one (20%) patient for deterioration in ABG values 89 h into NPPV. None developed complications.

Patients With Pulmonary Edema: Eight patients were admitted to the ICU with pulmonary edema and respiratory failure or insufficiency. Their mean (±SD) age was 72±11 years; six were male. Findings prior to instituting NPPV were pH of 7.31±0.01, PaCO₂ of 40±8, PaO₂:FIO₂ of 157±115, RR of 31±7, HR of 104±16, and dyspnea score of 3.5±0.8. One (13%) patient failed to improve ABG values. Duration of NPPV was 15±16 h. Intubation was necessary in four (50%) patients for the following reasons: hemodynamic instability (2), inability to improve ABG values (1), and intolerance to the mask (1). One patient developed complications.

Predictors of Response

The following variables were analyzed for each group of ARF (1 to 5) to predict ABG response and likelihood for intubation: (A) at entrance into the study: (1) age, (2) use of accessory muscles of respiration or presence of paradoxical abdominal motion, (3) condition precipitating ARF, and (4) APACHE II score and predicted mortality; (B) at entrance and over time: (1) RR, (2) HR, (3) dyspnea score, (4) PaO₂:FIO₂, (5) pH, (6) PaCO₂, (7) PSV requirements, (8) exhaled VT, and (9) VE. No variable was found to predict the need for ETI in either the whole group or any subgroup of ARF. Variables predicting ABG response were found for hypercapnic patients (groups 2 and 3), but not for the one with hypoxemic failure (group 1). In patients with hypercapnic failure (group 2), baseline PaCO₂ (p=0.004) was significantly higher in nonresponders (Fig 6). In the combined hypercapnic groups (2 and 3) responders had a higher amount of applied PSV than nonresponders (15±4 vs 12±2; p=0.016). As shown in Table 7, reduction in PaCO₂ and rise of pH within 2 h of NPPV in groups 2 and 3 predicted successful response (p<.0001), but not necessarily intubation. Failure to identify variables predictive of ABG response and likelihood for intubation may reflect a lack of power or be indicative that the true predictive variables are characteristics of patients at enrollment or during the clinical course that were not recorded.

Table 7—Differences Between Responders and Nonresponders in Patients With Hypercapnic Failure and Insufficiency Combined

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Responders</th>
<th>Nonresponders</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>62</td>
<td>12</td>
<td>—</td>
</tr>
<tr>
<td>Age, yr</td>
<td>62±14</td>
<td>68±5</td>
<td>0.06</td>
</tr>
<tr>
<td>APACHE II</td>
<td>18±6</td>
<td>20±4</td>
<td>0.21</td>
</tr>
<tr>
<td>COPD, exacerbation</td>
<td>24</td>
<td>6</td>
<td>0.53</td>
</tr>
<tr>
<td>COPD, pneumonia</td>
<td>13</td>
<td>2</td>
<td>0.75</td>
</tr>
<tr>
<td>COPD, heart failure</td>
<td>5</td>
<td>3</td>
<td>0.11</td>
</tr>
<tr>
<td>pH*</td>
<td>7.26±0.06</td>
<td>7.27±0.06</td>
<td>0.3</td>
</tr>
<tr>
<td>PaCO₂, mm Hg*</td>
<td>75±17</td>
<td>77±26</td>
<td>0.6</td>
</tr>
<tr>
<td>PaO₂:FIO₂*</td>
<td>206±90</td>
<td>256±149</td>
<td>0.13</td>
</tr>
<tr>
<td>RR*</td>
<td>29±8</td>
<td>27±10</td>
<td>0.135</td>
</tr>
<tr>
<td>Dyspnea score*</td>
<td>3.1±1</td>
<td>2.7±1.3</td>
<td>0.18</td>
</tr>
<tr>
<td>PSV, cm H₂O₁</td>
<td>15±4</td>
<td>12±2</td>
<td>0.016</td>
</tr>
<tr>
<td>Exhaled VT, mL₁</td>
<td>620±353</td>
<td>584±223</td>
<td>0.8</td>
</tr>
<tr>
<td>VT, L/min¹</td>
<td>10.1±6.4</td>
<td>13.1±8.2</td>
<td>0.5</td>
</tr>
<tr>
<td>≥2 h pH¹</td>
<td>7.33±0.07</td>
<td>7.22±0.05</td>
<td>0.0001</td>
</tr>
<tr>
<td>≥2 h PaCO₂₁</td>
<td>62±16</td>
<td>90±22</td>
<td>0.0001</td>
</tr>
<tr>
<td>≥2 h PaO₂:FIO₂¹</td>
<td>259±128</td>
<td>208±49</td>
<td>0.23</td>
</tr>
<tr>
<td>≥2 h RR¹</td>
<td>22±9</td>
<td>24±9</td>
<td>0.54</td>
</tr>
<tr>
<td>≥2 h Dyspnea score¹</td>
<td>2±1.1</td>
<td>2±0.9</td>
<td>0.96</td>
</tr>
</tbody>
</table>

*Values obtained at initiation of NPPV.
†Values obtained within 2 h of NPPV.

Discussion

To our knowledge, the present study is the largest published experience using NPPV as first-line intervention in a heterogeneous population of patients with ARF. This study has limitations related to the reality of clinical investigation in a teaching center. Many of the patients with ARF admitted to the ICU were already intubated in the emergency department or the ward. Despite this, in the last 14 months of the study, 36% of all patients with ARF received NPPV. Over the 2-year period of the study, we had 48 teams of (three to five) physicians-in-training rotate through two busy medical ICUs. A dedicated RT provided an educational program at the beginning of each monthly rotation and, on weekdays, supervised the use of this technique during the daytime. No direct supervision was provided at night or weekends, and it is possible that the sickest patients had no attempt at NPPV by the on-duty physician in training. When patients with ARF received NPPV, the response was similar to one of our prior, more controlled studies.1-3 In this regard, our experience is similar to that of Pennock et al10 in patients with postoperative respiratory failure, indicating that NPPV can be implemented effectively in clinical practice following a period of education and supervision.

The findings of this study provide strong support for using NPPV in selected patients with ARF. In reviewing several aspects of NPPV in ARF, we will compare our methods and results with the published experience of other groups.
Methodology

NPPV methodology in patients with respiratory failure has varied among centers, and little or no comparison has been made among different techniques. We will present the rationale for our institutional approach, which was modeled on the prior experience of groups treating patients with chronic respiratory failure.

Patient Selection: An alert and cooperative patient is critical for initiating NPPV. Patients with COPD and CO₂ narcosis, however, are an exception. In our and others’ experiences, most of these patients will improve mentation within 30 min of effective NPPV, and only a minority will require intubation. Although, extremely anxious patients may be better served by sedation and ETI, moderate degrees of anxiety are frequently overcome once a patient’s ventilatory needs are met. During NPPV, patients can achieve a level of control and independence totally different from when intubated, and sedation is rarely required. When necessary, we have found IV administration of a small dose (2 mg) of morphine sulphate to be very effective. NPPV should be avoided in patients with cardiovascular instability (hypotension or life-threatening arrhythmia), in those who require an ET to protect the airways (coma, acute abdominal processes, impaired swallowing), or have life-threatening refractory hypoxemia (PaO₂<60 mm Hg on 1.0 FIO₂).

Interface: Most studies have utilized a nasal mask. Nasal masks add less dead-space, cause less claustrophobia (rare occurrence), minimize potential complications if vomiting occurs (rare occurrence), and allow for both expectoration and oral intake without removing the mask. However, a facial mask is preferable because dyspneic patients are mouth breathers, mouth breathing bypasses resistances of the nasal passages, and mouth opening during nasal mask ventilation results in air leakage and decreased effectiveness. Although to our knowledge no study has directly compared their efficacy, one group has reported a higher success with face mask NPPV vs their institutional historical control with nasal mask. Improvement in ABG values appears to be slower in some of the studies utilizing a nasal mask in comparison to those using a face mask. We believe a face mask is best suited for patients with severe ARF and dyspnea. The dead-space volumes of a facial and a nasal mask are 250 mL and 105 mL, respectively. Dead-space volume from the mask and the oropharynx does not appear to affect the effectiveness of ventilation.

Comfort: Since patient tolerance is essential to the success of NPPV, a tight, uncomfortable fit should be avoided. Even in patients with hypoxemic respiratory failure on CPAP, a small leak will not cause airway pressure to drop. When securing the mask, we allow enough space to pass two fingers beneath the head straps. Masks with a rubber or air cushion (list of makers available from us on request) fit most facial contours and do not require tight strapping. Small degrees of air leakage are well tolerated if the returned Vt is adequate (≥7 mL/kg). Similar to others, we have often found that proper fitting of the mask is difficult in edentulous patients and in those with beard. Placement of a nasogastric tube is indicated only for patients developing gastric distention (see below) or to provide access for enteral feeding.

Mechanical Ventilation: Most studies used pressure-limited ventilation delivered by a broad range of ventilators. Inspiratory PSV improves the efficacy of spontaneous breathing by allowing an optimal synchrony between patient effort and delivered assistance. In comparison to volume-cycled ventilation, PSV minimizes peak inspiratory mask pressure and air leakage. Although Vt may vary as a function of change in airway resistance and compliance, this variance has been an uncommon problem in our experience. In one comparison study with assist-control ventilation, PSV was equally effective in improving gas exchange but was better tolerated and associated with fewer complications.

The physiologic effects of NPPV with PSV have been described. With mask ventilation, Vr, gas exchange, RR, and diaphragmatic activity are improved in proportion to the amount of pressure applied. In our protocol, we have adjusted PSV at the start of NPPV to obtain a Vr of 7 mL/kg or more (Fig 1). In most patients, this Vr target was well tolerated and was adequate for resting respiratory muscles and improving gas exchange (see below). We believe that PSV should be adjusted, as soon as the patient can tolerate it, to obtain the largest exhaled tidal volume (PSV max). When excessive pressure is applied, activation of expiratory abdominal muscles to terminate flow can be observed. When significant air leakage occurs, CPAP first and then PSV (or Vr) should be decreased to reduce peak mask pressure.

Similar to our approach, most studies delivered MV continuously until resolution of ARF. Some groups, treating less severe forms of respiratory failure, have delivered NPPV for a few hours a day over extended periods of time. Since mask ventilation provides a great degree of flexibility, it can be best adjusted to meet a patient’s individual needs. In some of our patients with COPD and mild forms of respiratory acidosis, nocturnal ventilation was continued for a few days following resolution of respiratory failure. Mask ventilation is easy to administer and to discontinue. In the short-term setting, it is less time-consuming than intubation and avoids the acute complications associated with placing an ET. Aspiration has been documented in up to 27% of patients during intubation. During weaning, NPPV eliminates the “reintubation
factor” associated with premature removal of ventilation.

In our experience, the first hour of NPPV is labor intensive. Bedside presence of a RT or nurse familiar with this mode of ventilation is essential for adjustments of the mask and the ventilator’s settings. Providing reassurance and adequate explanation to the patient about what to expect is of utmost importance. Patients are instructed to call the nurse if they develop abdominal distention or nausea/vomiting or need to remove the mask to expectorate. Monitoring RR, exhaled Vt, oxygen saturation, use of the accessory muscle of respiration (visual or palpation\(^3\)), dyspnea level, mental status, comfort, and ABG values allows the observer to assess a patient’s response and likelihood of success. Patients showing an improvement in gas exchange in the first hour of NPPV are more likely to avoid intubation (see below). In our experience, after the first hour of uncomplicated NPPV, most patients do not require bedside observation; ventilator and oximetry alarms provide warnings for early intervention if it becomes necessary. We have found that time involvement with NPPV is proportional to the level of experience, and this may explain the findings of others.\(^5\) In stable patients, intermittent 15-min periods off NPPV can be provided for oral intake. The mask can be removed as needed for expectoration.

Response to NPPV

In agreement with the literature, we have found NPPV to be an effective and safe modality for ventilatory support of a heterogeneous population of patients with ARF. Furthermore, with this large study, we have confirmed several important prior observations showing definitive advantages of NPPV when compared with conventional ventilation with ETI. In this study, NPPV rapidly improved gas exchange abnormalities in most patients with hypercapnia (84%) and hypoxemia (75%), and only 20 (15%) patients required intubation for their inability to improve ABG values. Tachypnea and dyspnea improved soon after instituting NPPV irrespective of ABG response. NPPV was well tolerated, was associated with minimal complications, and entailed a short period of ventilation.

Complications: In a controlled ICU environment, postponement of intubation in patients failing an initial approach with NPPV was not associated with serious adverse events. This important observation is in agreement with the literature. Our findings confirm the previously reported low rate of complications associated with NPPV.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^9\)\(^,\)\(^14\)\(^,\)\(^16\)\(^,\)\(^24\)\(^,\)\(^28\)\(^,\)\(^31\)\(^,\)\(^32\) We have not identified risk factors for FSN, which occurred in 13% of patients. Only three patients (2%) developed gastric distention and required insertion of a nasogastric tube for suction. None of them vomited or aspirated. Delivery of a peak positive pressure below the resting upper esophageal sphincter pressure (33±12 mm Hg)\(^41\) appears safe in avoiding gastric insufflation. Despite the low incidence of gastric distention, nurses and therapists should be instructed to examine patients for signs of abdominal distention.

Pneumonia is a rare complication of NPPV.\(^1\)\(^,\)\(^20\) In our collective experience of more than 200 patients, pneumonia occurred in only 2 patients. This is a significantly lower incidence than the one of intubated patients (11%) from our own institution.\(^42\) Possible mechanisms were previously described.\(^1\) By screening for development of fever, we have not detected other obvious infections. This low rate of infectious complications in patients receiving NPPV has been confirmed in randomized studies\(^13\)\(^,\)\(^20\) and contrasts sharply with the one detected in intubated patients.\(^42\)\(^,\)\(^43\) Lack of invasion by ET and other catheters and shorter duration of MV and ICU stay are the most likely explanations.\(^1\) Absence of barotrauma in this large patient population also agrees with prior studies.

Hypercapnic Respiratory Failure: In acute exacerbation of obstructive airways disease (OAD), excess work of breathing due to increased airway resistance and severe dynamic hyperinflation overwhelms the capacity of the respiratory muscles.\(^44\) Dynamic hyperinflation or intrinsic positive end-expiratory pressure (PEEPi) causes substantial shortening of the diaphragm and the inspiratory intercostal and accessory muscles, reducing their efficiency and endurance. Inspiratory muscle fatigue is thought to be the final common pathway that causes ventilatory failure in patients with OAD.\(^45\) Patients present with dyspnea and a high respiratory frequency. Most of the breaths are shallow, and much of the Vt is wasted as dead-space ventilation, resulting in retention of carbon dioxide and respiratory acidosis. When conventional therapy fails, MV is instituted to increase effective Vt, improve gas exchange, relieve respiratory distress, and rest the fatigued respiratory muscles. A large body of literature indicates that these objectives can be safely achieved with noninvasive ventilation in most COPD patients with hypercapnic respiratory failure. Furthermore, NPPV may lead to a significant reduction in morbidity, mortality, and ICU cost.\(^30\)

In patients with OAD (COPD and asthma) and ARF, the inspiratory effort is divided into two components. An isometric contraction of the inspiratory muscles to counterbalance PEEPi is followed by an isotonic contraction to generate inspiratory flow and Vt.\(^30\) Studies evaluating the effects of MV delivered by mask on the work of breathing and gas exchange in patients with OAD indicate that low-level CPAP (5 cm H\(_2\)O) offsets PEEPi and significantly reduces inspiratory work load.\(^30\)\(^,\)\(^46\)\(^,\)\(^47\) While intermittent positive pressure ventilation improves Vt, gas exchange, RR, and diaphragmatic activity in proportion to the amount of
pressure applied.\textsuperscript{5,36,38,39} It has been shown that suppression of diaphragmatic activity occurs within five to six NPPV breaths.\textsuperscript{36} In one study of patients with COPD and ventilatory failure, the mean peak pressure that resulted in the maximal reduction of diaphragmatic phasic EMG was 13.3±1.8 cm H\textsubscript{2}O.\textsuperscript{36} In another study, a PSV of 20 cm H\textsubscript{2}O, without application of CPAP, was more effective than 12 cm H\textsubscript{2}O.\textsuperscript{5}

After achieving an initial V\textsubscript{T} target of 7 mL/kg and a RR below 25 breaths/min, we suggest increasing delivered pressure (up to 20 to 25 cm H\textsubscript{2}O) to achieve the V\textsubscript{E} required to correct gas exchange abnormality. Mask leak, however, may be a limiting factor.

In agreement with the literature and our prior experience, we have found NPPV to be effective in improving effective alveolar ventilation and gas exchange (Fig 6) and in decreasing RR and respiratory distress. In responders, improvements in PaCO\textsubscript{2} and pH were rapid (Fig 6), similar to the findings of others.\textsuperscript{5,13} RR and dyspnea decreased irrespective of improvements in gas exchange. NPPV corrected or improved ABG values in 84% of cases and avoided ETI in 65%. The intubation rate in the literature has ranged from 9 to 40%.\textsuperscript{1,2,5,3,13,15,16,24} In our study, best results were obtained in COPD patients without pneumonia or congestive heart failure (Table 2). The higher rate of intubation among patients with hypercapnic insufficiency indicate that ABG value at entrance may not reflect severity of disease and rate of progression, but earlier intervention. Of importance, an inability to improve gas exchange (by the study criteria) did not invariably lead to ETI. Once dyspnea and tachypnea were improved, patients did not require ETI if respiratory acidosis was improved but not necessarily corrected (pH≥7.35). However, 18% of patients required ETI despite improvements in gas exchange. Mortality rate was 7%, similar to our prior report.\textsuperscript{1}

We have searched for variables to predict ABG response and need for intubation in patients receiving NPPV for either RF (group 2) or insufficiency (group 3). In the combined groups, no differences were found at entrance (Table 7). In the hypercapnic failure group, however, nonresponders had a higher PaCO\textsubscript{2} at intiation of NPPV (91.5±4.2 vs 80±1.5; p<0.001). Other studies have found no variable at initiation of NPPV that discriminated success from failure.\textsuperscript{1,4,6,13-16} Two reports found the APACHE II score\textsuperscript{30} or the Simplified Acute Physiologic Score\textsuperscript{17} to have predicted value for intubation, but this was not confirmed by our findings. Similar to our prior report, a reduction in PaCO\textsubscript{2} or pH within 1 to 2 h of NPPV predicted a sustained improvement in gas exchange.\textsuperscript{1} In two studies, an inability to improve PaCO\textsubscript{2} was related to mask (nasal) leak.\textsuperscript{25,30} It is possible that improving the interface may lead to higher efficacy of NPPV. In our study, nonresponders received a lower amount of PSV (12±2 vs 15±4; p<0.016), which was inadequate in improving gas exchange despite obtaining a returned V\textsubscript{T} and V\textsubscript{E} similar to responders. Since not all hypercapnic patients failing to improve ABG values required ETI, we cannot arbitrarily suggest intubating all those who fail to improve within 2 h of NPPV, especially when other clinical parameters improve.

Mean duration of MV in this study was 25 h, similar to our prior reports.\textsuperscript{1,3} It is not readily explainable why the duration of MV delivered by noninvasive means is significantly shorter than traditional MV via ETI. This finding is similar to one of other groups.\textsuperscript{20,25} Of interest, the short duration of continuous, successful NPPV is consistently seen across all types of RF in this study. This may indicate an intrinsic advantage of NPPV irrespective of the specific characteristics of various forms of ARF. Factors that may be involved in shortening the duration of MV include earlier intervention, avoidance of sedation and paralysis, lower rate of nosocomial infections and other complications, elimination of the work of breathing related to the ET, and earlier removal.

Comparison with historical control\textsuperscript{15,15} or the literature\textsuperscript{16} has suggested a significant reduction in need for ETI, duration of MV, ICU stay, and mortality rate in COPD patients receiving NPPV vs those receiving conventional treatment. Six recent randomized studies (113 patients received NPPV and 107 received conventional treatment) have confirmed these observations.\textsuperscript{18-20,23,25,31} The largest study, a multicenter European trial, evaluated early use of face mask NPPV in 85 COPD patients with acute exacerbation. Patients randomized to NPPV had a significantly lower intubation rate (26% vs 74%; p<0.001), length of hospitalization (23±17 vs 35±33 days; p<0.005), and mortality rate (9% vs 29%; p=0.02) when compared with the control group treated with conventional therapy.\textsuperscript{20} Of significance, mortality rate was similar among intubated patients in the two groups. In our study, mortality rate was 20% in intubated patients irrespective of their ABG response to NPPV. In a similar group of COPD patient, Kramer et al\textsuperscript{24} reported an intubation rate of 9% in those randomized to NPPV (nasal bilevel positive airway pressure [BiPAP]) vs 67% in the control group (p=0.017). Overall, the low risk associated with postponing ETI in these monitored patients, we believe, justifies implementing NPPV as first-line intervention in eligible COPD patients with ARF. The result of this study indicates that COPD patients with pneumonia or congestive heart failure have a higher rate of failure and require closer monitoring.

Five patients in our study had status asthmaticus with severe respiratory acidosis. Intubation was avoided in four. Mask CPAP has been shown to reduce the load of breathing and to improve inspiratory muscle efficiency in asthmatics.\textsuperscript{46,48} Status asthmaticus was a
contraindication to NPPV in other studies\(^6\) and cannot be recommended as an indication for NPPV from this limited experience. The results are encouraging despite the severity of ARF (pH \(7.24 \pm 0.08\) and PaCO\(_2\) \(67 \pm 13\) mm Hg) and are similar to our prior report (two patients).\(^1\) Managing secretions was not a problem, and the intervention was tolerated better than conventional ventilation in those patients who had been intubated during prior episodes of ARF. Conventional mechanical ventilation in patients with asthma is frequently associated with many complications.\(^49\) Furthermore, placing an ET in patients with hyperreactive airways may induce bronchospasm. With NPPV, we were able to achieve rapid correction of gas exchange without using high ventilatory pressures, indicating that the ET may contribute to the increased resistance and higher peak pressures.

**Hypoxemic Respiratory Failure:** Acute hypoxemic respiratory failure can be short lasting (cardiogenic pulmonary edema, atelectasis) or prolonged (ARDS). ETI is required for patients with ARF who are expected to require prolonged ventilatory support or who are hemodynamically unstable. Positive airway pressure, either continuous (CPAP) or PEEP, is used for recruiting underventilated alveoli by increasing lung volume at end expiration, resulting in improved gas exchange. CPAP, applied noninvasively through a mask, has been used successfully for years to correct refractory hypoxemia in patients with cardiogenic and noncardiogenic pulmonary edema.\(^50\) Retention of carbon dioxide has occasionally been a limiting factor for this technique.

Adding intermittent positive pressure ventilation to CPAP improves gas exchange by increasing mean airway pressure, the most important determinant of blood oxygenation in patients with diffuse lung disease.\(^51\) In the literature, NPPV for hypoxemic ARF was described in 12 studies.\(^1,3,6,7,9,10,12,13,17,18,24\) The overall success rate in avoiding intubation varied from 40 to 93%. Patients with postoperative ARF\(^9,10\) and pulmonary edema\(^13\) appeared to do better than the one with pneumonia.\(^15\) In the present study, we evaluated 41 patients with severe hypoxemic RF (PaO\(_2\):FIO\(_2\) = 110±46) of diverse etiologies (Table 2). Patients required a high Ve (17 L/min). Gas exchange improved in 75% of patients. In responders, NPPV was effective in reducing RR and dyspnea. We found no variable to predict success of NPPV in hypoxic patients. The three leading causes of hypoxic ARF are addressed separately.

NPPV was highly effective in 11 AIDS patients with opportunistic pneumonia and severe hypoxemia. Two (20%) patients failed to improve ABG values and required intubation. Duration of NPPV was longer than in other conditions causing hypoxic ARF, but still safe and well tolerated. To our knowledge, there are no prior reports of NPPV in patients with AIDS; however, the use of a CPAP mask has been described in prior studies with excellent results.\(^52-54\)

Favorable results were also seen in patients with severe CAP, with (27) or without COPD (14). NPPV improved gas exchange in more than 75% of patients and avoided intubation in 62%. This rate of intubation is similar to one prior report\(^14\) and significantly better than others.\(^13,17,18\) A small number (three) required intubation for inability to clear secretions. The value of positive pressure by mask in removal of bronchial secretions was previously described.\(^55\) Actual mortality (17%) was lower than predicted (36%). These data indicate that NPPV may be safely applied to patients with pneumonia and ARF, provided that the patient is capable of effectively expectorating secretions.

NPPV was effective in improving gas exchange in all but one patient with pulmonary edema who required intubation. Hemodynamic instability led to intubating of two patients. Duration of NPPV was shorter than other forms of ARF. These findings are in agreement with those of other groups.\(^9,13,14\) The value of mask CPAP in a patient with pulmonary edema meeting criteria for intubation was proved in a recent randomized study.\(^56\) A study comparing CPAP alone vs CPAP with intermittent positive pressure in patients with pulmonary edema is necessary.

**Postextubation Respiratory Failure:** Five prior studies,\(^1,13,17,18,28\) reported using NPPV in patients with postextubation RF due to either respiratory muscle fatigue or upper airway obstruction. The overall success rate was 81%. In postextubation ARF, we have found the face mask to be equally effective to the ET in delivering the mechanical tidal breath.\(^1\) In the present study, 39 patients developed postextubation RF. NPPV was effective in improving or correcting ABG values in 31 (86%) and in avoiding reintubation in 65%. None of the patients developed nosocomial pneumonia, which may occur with increased incidence in reintubated patients.\(^57\) Three patients had (partial) upper airway obstruction and were supported with NPPV for a mean of 18 h, while receiving treatment with racemic epinephrine and systemic corticosteroids. Recent reports indicate that NPPV may have a role in patients who are difficult to wean.\(^27,55,59\)

**Patients Who Refuse or Are Not Candidates for ETI:** Four prior studies have reported on the use of NPPV in patients with ARF who are poor candidates for ETI for a variety of reasons: advanced age or poor physiologic condition (n=42),\(^14,50\) terminally ill patients (n=11),\(^3\) and those with advanced directives (do not resuscitate status) (n=8).\(^21\) The overall success rate was 62%, i.e., of these terminally ill patients, 38 of 61 would otherwise have died had they not been placed on a regimen of noninvasive ventilation. These findings agree with those of the present study. This method
should be strongly considered in patients with advanced disease who appear to have a reversible cause of RF. Among our successfully treated patients, many survived for years of quality life after hospital discharge. NPPV has also been described for patients with terminal RF. This modality was well tolerated and prolonged life a few extra days, thus allowing life closure tasks to be completed. An editorial accompanied this publication warning of the potential ethical and economic cost of delaying the inevitable in patients with terminal RF.

**CONCLUSION**

The findings of this large prospective observational study confirm our and others’ previous reports on the effectiveness of NPPV in correcting gas exchange abnormalities and avoiding intubation in selected patients with ARF. The protocol was simple to implement and monitor. Education of physicians in training and direct supervision by an experienced RT were essential to the success of the project. NPPV proved to be effective, comfortable, and safe. Duration of ventilation was short, confirming previous reports that NPPV decreases the length of MV in patients with ARF. Postponing intubation had no serious consequences. In our medical ICUs, NPPV has become the preferred initial treatment of patients with hypercapnic ARF and in those with hypoxemic ARF in whom the clinical condition can be readily reversed (48 to 72 h), when airway control is not needed, and the patient is hemodynamically and electrocardiographically stable.

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