The Effect of Body Mass Index on Outcomes of Patients Receiving Noninvasive Positive-Pressure Ventilation in Acute Respiratory Failure

Deborah A Hutter MD, Bart K Holland PhD, and Hormoz Ashtyani MD

BACKGROUND: A study was undertaken to determine factors present in adult patients, newly admitted to the hospital, that predict the inability of noninvasive positive-pressure ventilation (NPPV) to sustain the work of breathing and avoid endotracheal intubation. METHODS: Data were collected prospectively from patients with acute respiratory failure who were admitted to Hackensack University Medical Center from August 2001 to August 2002 and received NPPV. Physiologic characteristics of those patients on admission were compiled into a database, with the hypothesis that those with the worst initial physiologic characteristics would subsequently fail NPPV and require endotracheal intubation with mechanical ventilation. RESULTS: Seventy-five patients were included. Sixty-four patients (85%) successfully avoided endotracheal intubation and were discharged. Of the 11 patients who failed NPPV, 8 were intubated and 5 expired. The groups were comparable in age, sex, arterial blood gases, and Acute Physiology and Chronic Health Evaluation score (p > 0.05). The success group, however, had a significantly higher body mass index (29 kg/m² vs 23 kg/m², p = 0.0167). CONCLUSIONS: The following can be concluded from our study: there is a low failure rate for NPPV (15%); patients with a low body mass index are more likely to fail NPPV and require endotracheal intubation; and patients who fail NPPV have a higher risk of mortality (p = 0.00016). Key words: noninvasive ventilation, respiratory failure, body mass index, endotracheal intubation, hypoxemia. [Respir Care 2004;49(11):1320–1325. © 2004 Daedalus Enterprises]
of patients with ARF include arterial pH\(^1\) and Acute Physiology and Chronic Health Evaluation (APACHE II) score.\(^{19,20}\) Factors that affect the successful use of NPPV have included oxygenation\(^{21}\) and degree of hypercapnia.\(^{22–27}\)

We performed a prospective, observational study with patients in ARF who were placed on NPPV. We compiled each patient’s age, sex, APACHE II score, body mass index, and worst pre-ventilation arterial blood gas values on admission into a database. We hypothesized that patients with the worst physiologic factors at their baseline evaluation would be the most likely to fail NPPV and require endotracheal intubation and mechanical ventilation. We then compared physiologic factors to determine if there was any association between physiologic factors present on admission and the outcome of NPPV in patients in ARF.

### Methods

#### Study Design

Following the approval of our institutional review board, we performed a prospective cohort study of adult patients in ARF who were initially treated with NPPV within 48 hours of admission, from August 2001 to August 2002. This study was conducted at Hackensack University Medical Center, a 700-bed tertiary university medical center with a fellowship program in pulmonary, critical care, and sleep medicine.

#### Subjects

Informed consent was obtained from all patients for data collection within 48 hours of admission. All patients who were prescribed NPPV within 48 hours were screened for entrance into the study. Patients were recruited who were initially diagnosed with ARF and were empirically placed on NPPV, with oronasal masks, using a bi-level positive airway pressure ventilator (BiPAP ST-D, Respiromics, Murrysville, Pennsylvania) within 48 hours of admission. ARF was defined as an inability to sustain the work of breathing, as evidenced by accessory muscle use, altered mental status, and at least one of the following: respiratory rate > 16 breaths/min, hypoxia (ratio of arterial partial pressure of oxygen to fraction of inspired oxygen \(\frac{PaO_2}{FiO_2}\) < 250 mm Hg), and/or hypercapnia (\(PaCO_2\) > 45 mm Hg) (Table 1). Patients were excluded if they used NPPV at home and were continuing therapy, or if they had been intubated on admission or in the previous 48 hours. Patients were not excluded on the basis of race, sex, respiratory status, or admitting diagnosis. They were admitted consecutively to the study, either from the emergency room, the intensive care unit, or the general medical floor. All patients received positive-pressure ventilation within 48 hours of admission. All patients also received medications to treat their underlying illness, which could include antibiotics, bronchodilators, vasopressors, and diuretics. Patients who were admitted to the hospital with ARF and who had been intubated by emergency medical services personnel in the field were excluded, because they were not given a trial of NPPV.

#### NPPV Application

All patients had NPPV ordered and adjusted by board-certified pulmonologists not directly involved with the study. All patients received NPPV via continuous positive airway pressure or bi-level mode with a BiPAP S/T-D 30 ventilator for a minimum of 2 hours of therapy. Oronasal masks were fitted by trained respiratory therapists, using fit guides provided by Resmed (Poway, California). Straps

### Table 1. Identified Causes of Respiratory Failure (\(n = 75\))

<table>
<thead>
<tr>
<th>CHF/COPD</th>
<th>CHF</th>
<th>COPD</th>
<th>Pneumonia</th>
<th>NMS</th>
<th>Surgical</th>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success</td>
<td>Failure</td>
<td>Success</td>
<td>Failure</td>
<td>Success</td>
<td>Failure</td>
<td>Success</td>
</tr>
<tr>
<td>Number of patients</td>
<td>21</td>
<td>1</td>
<td>15</td>
<td>3</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Age (y)</td>
<td>68</td>
<td>81</td>
<td>76</td>
<td>70</td>
<td>64</td>
<td>72</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>31</td>
<td>29</td>
<td>30</td>
<td>18</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>(PaCO_2) (mm Hg)</td>
<td>60</td>
<td>48</td>
<td>52</td>
<td>60</td>
<td>63</td>
<td>67</td>
</tr>
<tr>
<td>(PaO_2/FiO_2) (mm Hg)</td>
<td>235</td>
<td>262</td>
<td>219</td>
<td>151</td>
<td>211</td>
<td>176</td>
</tr>
</tbody>
</table>

\*Values are means

CHF = congestive heart failure
COPD = chronic obstructive pulmonary disease
NMS = neurologic or musculoskeletal disorder
Surgical = surgical disorder or trauma
Renal = renal failure requiring dialysis
BMI = body mass index (body weight in kilograms divided by squared height in meters)
\(PaO_2/FiO_2\) = ratio of arterial partial pressure of oxygen to fraction of inspired oxygen
were adjusted to allow 1–2 fingers to pass easily between the straps and the patient’s face. Soft nasal cushioning was provided as necessary to prevent skin necrosis. Initial settings were empirically chosen by pulmonologists. Patients were initiated on a pressure of > 5 cm H2O and then titrated by respiratory therapists for patient comfort and to keep the patient’s respiratory rate < 35 breaths/min and oxygen saturation (measured by pulse oximetry) > 92%. Masks and settings were adjusted to achieve the least air leak (goal of < 10 L/min). Mask leak was quantified with a pneumotachograph and compensated for by the pressure-controlling valve.

The need for endotracheal intubation and mechanical ventilation was decided on a case-by-case basis by the pulmonologist caring for the patient.

**Data Collection**

A standardized form was used to collect data from all of the charts. Data collected included date of admission, NPPV orders, age, race, sex, body mass index, APACHE II score, admitting blood gas, supplemental oxygen use, documentation of the need for intubation, actual intubation, and mortality. Admitting blood gas was defined as the worst arterial blood gas obtained within 24–48 hours of admission and prior to ventilation. APACHE II scores were calculated using standard formulas.\(^{19}\) Body mass index was calculated as body weight in kilograms divided by the squared height in meters.

**End Points**

Patients were identified as having a successful application of NPPV if they were not intubated during the hospitalization and were alive at the time of discharge. Patients were identified as failing NPPV if they had endotracheal intubation performed subsequent to the application of NPPV, or if the pulmonologist in attendance decided to proceed with intubation, and this was subsequently refused by the patient.

**Analysis**

The primary end point in this study was the need for endotracheal intubation and/or mortality. A comparison was performed between the group successfully recovering respiratory function following NPPV and the group failing this intervention and requiring endotracheal intubation. Nonparametric statistics were performed using SAS software (SAS Institute, Cary, North Carolina). A univariate analysis was performed to determine the single most important variable. The variables compared between the 2 groups included age, sex, body mass index, APACHE II score, $P_{aO_2}/F_{I O_2}$, pH, and $P_{aco_2}$. The chi-square test was used to analyze the statistical significance of the difference between the 2 groups. Fisher’s exact test was used to determine the statistical significance of the number of men and women, and differences in race, in both groups. The joint effects of all variables at one time are usually combined in the APACHE II score. Since the APACHE II score was included as a variable, this prohibited a true multivariate analysis. However, logistic regression was used to examine this effect. Differences were considered significant if the p value was < 0.05.

**Results**

Seventy-five patients were enrolled in the study. There was a diversity of admitting diagnoses, and most patients had a combination of chronic obstructive pulmonary disease and congestive heart failure (see Table 1). Other diagnoses included asthma, sepsis, aspiration pneumonia, restrictive lung disease, and shock (see Table 1). NPPV was successful in avoiding endotracheal intubation in 64 patients (85%) with ARF who were subsequently discharged from the hospital.

The duration of NPPV use from time of onset to time of failure ranged from 2 hours of continuous use to as much as 30 days of intermittent use (15-min to 12-h breaks, as tolerated by patients). The mean settings used were inspiratory pressure 12 cm H2O and expiratory pressure 6 cm H2O, with 6 L/min oxygen (ranged from 2 L/min to 15 L/min). Most patients in the study received bi-level positive-pressure ventilation; this study was not powered to compare differences between constant and bi-level pressure ventilation. Reasons for intubation included overt respiratory distress, lack of improvement of gas exchange, and unresolving hypoxia (Table 2). The patients were approximately in their eighth decade of life (mean age of 75), and the 2 groups had approximately the same APACHE II scores (17 in NPPV success group vs 19 in NPPV failure group) (see Table 2). The logistic regression model showed that for every 1-point increase in APACHE II score, there was a 9% increase in risk of endotracheal intubation and mechanical ventilation. That difference was not statistically significant. APACHE II score could not be used to identify those who would require intubation or those with a higher risk of mortality.

There was no statistically significant difference in the distribution of patients in the success group or failure group by age, sex, or race (by Fisher’s exact test). Of the 11 patients who failed NPPV, 8 were intubated and 5 subsequently died (5/8 or 62.5% of those intubated). There was also a tendency for patients in the failure group to have a slightly lower $P_{aO_2}/F_{I O_2}$ (173 vs 229 mm Hg), but that difference also was not statistically significant (p = 0.086). There were also no statistically significant differences between the groups in respiratory rate (26 breaths/min vs 29
The variable with the strongest association with failure of NPPV and the need for intubation was body mass index. The mean body mass index in the group with the successful application of NPPV was 29 kg/m², whereas the mean body mass index of the group requiring intubation was 23 kg/m² (p = 0.0167). Patients in the failure group also had a tendency to have worse oxygenation, but that difference was also seen in the studies performed by Meduri et al.2,5 The higher mortality seen with endotracheal intubation and mechanical ventilation has been attributed to the acquisition of ventilator-associated pneumonia or being more ill in ways not easily identifiable (such as ventilatory asynchrony or less physiologic reserve); however, that does not completely explain the difference.

Few studies have looked at the characteristics of patients who are unable to successfully avoid intubation by the use of NPPV.1,29 Meduri et al showed that nonresponders to NPPV who require intubation can be predicted by a PaCO₂ > 80 mm Hg or a PaO₂/FIO₂ < 150 mm Hg on an arterial blood gas analysis performed 2 hours after the initiation of therapy.2 Whether intubation prior to that decision point can alter the prognosis has not been examined. Our study, given its limitations, showed that arterial oxygenation, arterial carbon dioxide level, and serum bicarbonate did not predict the success or failure of NPPV (p = 0.086, 0.21, and 0.47, respectively).

In a study by Confalonieri, an APACHE II score of ≥ 29 was also associated with the failure of NPPV and the requirement for endotracheal intubation.29 In our study, only 1 patient had an APACHE II score > 29 and that

### Table 2. Characteristics of the Study Groups (n = 75)

<table>
<thead>
<tr>
<th></th>
<th>Success</th>
<th>Range</th>
<th>Failure</th>
<th>Range</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (y)</strong></td>
<td>70 ± 12</td>
<td>42–98</td>
<td>75 ± 9</td>
<td>59–91</td>
<td>0.326</td>
</tr>
<tr>
<td>Male/female (n)</td>
<td>30/34</td>
<td>NA</td>
<td>5/6</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>29 ± 8</td>
<td>16–50</td>
<td>23 ± 5</td>
<td>16–35</td>
<td>0.0167*</td>
</tr>
<tr>
<td><strong>APACHE II score</strong></td>
<td>17 ± 4</td>
<td>7–32</td>
<td>19 ± 4</td>
<td>11–25</td>
<td>0.177</td>
</tr>
<tr>
<td><strong>f (breaths/min)</strong></td>
<td>26 ± 6</td>
<td>18–51</td>
<td>29 ± 8</td>
<td>20–47</td>
<td>0.247</td>
</tr>
<tr>
<td><strong>HCO₃⁻ (mEq/dL)</strong></td>
<td>29 ± 6</td>
<td>15–40</td>
<td>28 ± 6</td>
<td>17–39</td>
<td>0.471</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>7.33 ± 0.08</td>
<td>7.08–7.48</td>
<td>7.38 ± 0.08</td>
<td>7.26–7.53</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>Paco₂ (mm Hg)</strong></td>
<td>61 ± 19</td>
<td>21–107</td>
<td>54 ± 15</td>
<td>41–92</td>
<td>0.206</td>
</tr>
<tr>
<td><strong>PaO₂/FIO₂ (mm Hg)</strong></td>
<td>229 ± 100</td>
<td>65–513</td>
<td>173 ± 78</td>
<td>54–272</td>
<td>0.0864</td>
</tr>
<tr>
<td><strong>IPAP (cm H₂O)</strong></td>
<td>10 ± 2</td>
<td>5–18</td>
<td>11 ± 2</td>
<td>8–15</td>
<td>0.497</td>
</tr>
<tr>
<td><strong>EPAP (cm H₂O)</strong></td>
<td>5 ± 2</td>
<td>3–14</td>
<td>5 ± 1</td>
<td>4–10</td>
<td>0.786</td>
</tr>
<tr>
<td><strong>Supplemental oxygen (L/min)</strong></td>
<td>6 ± 4</td>
<td>0–15</td>
<td>9 ± 5</td>
<td>2–15</td>
<td>0.0584</td>
</tr>
<tr>
<td><strong>Backup rate (breaths/min)</strong></td>
<td>13 ± 2</td>
<td>10–24</td>
<td>12 ± 2</td>
<td>8–16</td>
<td>0.413</td>
</tr>
</tbody>
</table>

NA = not applicable
BMI = body mass index (body weight in kilograms divided by squared height in meters)
*p < 0.05
APACHE = Acute Physiology and Chronic Health Evaluation
f = respiratory rate
HCO₃⁻ = serum bicarbonate
pH = arterial pH
Paco₂/Fio₂ = ratio of arterial partial pressure of oxygen to fraction of inspired oxygen
IPAP = inspiratory positive airway pressure
EPAP = expiratory positive airway pressure

Discussion

With the current expanded utilization of NPPV as an alternative to intubation and mechanical ventilation, the criteria for proceeding directly to intubation and endotracheal intubation have become less distinct.5,28 It is difficult to predict which patients will avoid endotracheal intubation by the use of NPPV, versus those who will ultimately need intubation and for whom the NPPV alternative is a potentially risky delay to providing more definitive therapy. The actual reasons that patients fail NPPV are not well delineated.

In our study only 2 of 11 patients were saved by rescue endotracheal intubation following the NPPV failure. Sixty-four of the 75 study patients in ARF did not need endotracheal intubation to maintain an adequate pulmonary toilet. Five patients underwent endotracheal intubation following NPPV and did not survive (62.5% of patients following rescue intubation), and that statistically significant difference was also seen in the studies performed by Meduri et al.2,5
patient did not require endotracheal intubation. There was no significant difference in APACHE II score between the group that avoided intubation and those who did not (p = 0.18). There was also no difference in outcome between patients with chronic obstructive pulmonary disease and those with congestive heart failure or a combination of those; however, our study may have been underpowered to detect such differences.

Another factor that has been used as a prognostic indicator is age. Unlike the studies performed by Meduri et al,2,5 we did not find a higher risk of failure of NPPV among patients over the age of 40. Our patient population included patients age 42–98 years, with an approximately equal group of men and women, and with overlapping diagnoses of congestive heart failure and chronic obstructive pulmonary disease (Table 3).

Logistic regression modeling was used to look for interactions between each of these variables. The difference in APACHE II score was not statistically significant, but the trend was intriguing. Because of the small sample size it is difficult to tell which single component is the driving force for that prediction. However, the proximate determinate of the trend may be body mass index. For each 1-point increase in body mass index there was a 29% decrease in the risk of endotracheal intubation and mechanical ventilation. These data do not show any similar trend related to hypoxia or hypercapnia.

Finally, the one factor that did have statistical significance in the outcome of NPPV was body mass index, which may be a reflection of muscle mass. The group that failed NPPV had a mean body mass index of 23 kg/m², which is relatively underweight. Poor nutritional status and lower muscle mass is a comorbidity that is difficult to identify and quantify. That lower muscle mass makes it more likely that a patient will become dependent on mechanical ventilation and less likely that the patient will have an effective cough. In fact, in critically ill patients it has been shown that patients in the overweight and obese categories may actually have better survival and discharge functional status.30 In a study by Celli et al, low body mass index in out-patients with chronic obstructive pulmonary disease was also shown to be a predictor of poor prognosis.31 Unfortunately, this is also a factor that is very difficult to modify with medical therapy. The reason for the association of low body mass index with the failure of NPPV is unclear. It may be that patients with lower body mass index require a different approach and methodology for the application of NPPV.

**Conclusions**

Our study was focused on delineating factors that would help to predict which patients NPPV would offer a safe alternative to endotracheal intubation. There appears to be a set of patients who are too sick to successfully sustain their work of breathing, but who can compensate safely with the assistance of NPPV. There is also a group of patients who will be unable to sustain the work of breathing even with the assistance of NPPV and will require intubation and mechanical ventilation. From our study, with our limited population, we have determined that there is a low failure rate for NPPV (15%), that patients who fail NPPV have an associated higher risk of mortality, and finally, that patients with a low body mass index may be more likely to fail NPPV and require endotracheal intubation. In summary, patients in ARF and who have intact airway defenses should be considered for a trial of NPPV; future studies are needed to better delineate the benefits and risks of this approach, as well as the methodology with which this device is applied.

**Table 3. Study Populations: Comparison With Results From Antonelli et al²⁸**

<table>
<thead>
<tr>
<th></th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subjects (n and %)</strong></td>
<td>Present Study*</td>
<td>Antonelli et al²⁸</td>
</tr>
<tr>
<td></td>
<td>64 (85)</td>
<td>246 (69)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>70 ± 12</td>
<td>58</td>
</tr>
<tr>
<td>Male/female (n)</td>
<td>30/34</td>
<td>158/88</td>
</tr>
<tr>
<td>Severity (mean ± SD)</td>
<td>17 ± 4 (APACHE II)</td>
<td>30 (SAPS II)</td>
</tr>
<tr>
<td>f (mean ± SD breaths/min)</td>
<td>26 ± 6</td>
<td>35</td>
</tr>
<tr>
<td>pH (mean ± SD)</td>
<td>7.33 ± 0.08</td>
<td>7.40</td>
</tr>
<tr>
<td>P_{aO2}/F_{IO2} (mean ± SD mm Hg)</td>
<td>229 ± 100</td>
<td>119</td>
</tr>
</tbody>
</table>

*The standard deviation values are only shown for the present study.

APACHE = Acute Physiology and Chronic Health Evaluation
SAPS II = Simplified Acute Physiology Score II
f = respiratory rate
pH = arterial pH
P_{aO2}/F_{IO2} = ratio of arterial partial pressure of oxygen to fraction of inspired oxygen
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REFERENCES


