Noninvasive Mechanical Ventilation in the Weaning of Patients with Respiratory Failure Due to Chronic Obstructive Pulmonary Disease

A Randomized, Controlled Trial

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Background: In patients with acute exacerbations of chronic obstructive pulmonary disease, mechanical ventilation is often needed. The rate of weaning failure is high in these patients, and prolonged mechanical ventilation increases intubation-associated complications.

Objective: To determine whether noninvasive ventilation improves the outcome of weaning from invasive mechanical ventilation.

Design: Multicenter, randomized trial.

Setting: Three respiratory intensive care units.

Patients: Intubated patients with chronic obstructive pulmonary disease and acute hypercapnic respiratory failure.

Intervention: A T-piece weaning trial was attempted 48 hours after intubation. If this failed, two methods of weaning were compared: 1) extubation and application of noninvasive pressure support ventilation by face mask and 2) invasive pressure support ventilation by an endotracheal tube.

Measurements: Arterial blood gases, duration of mechanical ventilation, time in the intensive care unit, occurrence of nosocomial pneumonia, and survival at 60 days.

Results: At admission, all patients had severe hypercapnic respiratory failure (mean pH, 7.18 ± 0.06; mean PaCO₂, 94.2 ± 24.2 mm Hg), sensory impairment, and similar clinical characteristics. At 60 days, 22 of 25 patients (88%) who were ventilated noninvasively were successfully weaned compared with 17 of 25 patients (68%) who were ventilated invasively. The mean duration of mechanical ventilation was 16.6 ± 11.8 days for the invasive ventilation group and 10.2 ± 6.8 days for the noninvasive ventilation group (P = 0.021). Among patients who received noninvasive ventilation, the probability of survival and weaning during ventilation was higher (P = 0.002) and time in the intensive care unit was shorter (15.1 ± 5.4 days compared with 240 ± 13.7 days for patients who received invasive ventilation; P = 0.005). Survival rates at 60 days differed (92% for patients who received noninvasive ventilation and 72% for patients who received invasive ventilation; P = 0.009). None of the patients weaned noninvasively developed nosocomial pneumonia, whereas 7 patients weaned invasively did.

Conclusions: Noninvasive pressure support ventilation during weaning reduces weaning time, shortens the time in the intensive care unit, decreases the incidence of nosocomial pneumonia, and improves 60-day survival rates.


Endotracheal intubation and mechanical ventilation are often needed in patients with acute exacerbations of chronic obstructive pulmonary disease. Respiratory muscle weakness, hypercapnia, hypoxia, and malnutrition are common in these patients, and they may receive prolonged mechanical ventilation, which has associated risks (1, 2). The duration of mechanical ventilation is influenced not only by the cause of disease but also by the ventilatory strategy chosen (3, 4). Patients receiving invasive ventilation are prone to developing nosocomial pneumonia and ventilator-associated pneumonia, with a high mortality rate (5-8).

Noninvasive ventilation may be a good alternative approach for patients with chronic obstructive pulmonary disease. However, in a recent multicenter study by Brochard and colleagues (9), only 29% of patients admitted to intensive care units were eligible for noninvasive ventilation. Nonetheless, noninvasive mechanical ventilation remains the "first line intervention in patients with hypercapnic respiratory failure" (10) in the absence of gross neurologic impairment. Some uncontrolled studies (11-13) have shown that noninvasive ventilation may also be useful in facilitating the weaning process in patients who require prolonged mechanical ventilation.

The aim of our multicenter, randomized study was to evaluate the effectiveness of a new weaning approach in patients with chronic obstructive pulmonary disease. This approach consisted of 24 to 48 hours of traditional ventilation delivered through an endotracheal tube followed by noninvasive pressure support ventilation. We compared the results obtained by using this strategy with those produced by using the same ventilatory mode delivered invasively. End points of the study were duration of mechanical ventilation, duration of intensive care unit stay, incidence of nosocomial pneumonia, and 60-day survival rate.

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721
Methods

Patients

A two-group, parallel, randomized, controlled trial was carried out in patients known to have chronic obstructive pulmonary disease. All patients known to have this disease who were admitted for acute relapse of their disease at three intensive care units and who needed intubation were eligible for the study. Acute relapse was defined as respiratory acidosis ($\text{pH} \leq 7.33$ while breathing room air); elevated bicarbonate levels; hypoxemia ($\text{PaO}_2 \leq 45 \text{ mm Hg}$ while breathing room air); and severe dyspnea in the absence of an objectively documented cause, such as pneumonia (14, 15) or 1 of 11 nonoperative respiratory diagnoses (excluding chronic obstructive pulmonary disease) found in the Acute Physiology, Age, and Chronic Health Evaluation (APACHE) III (16).

Fifty-six percent of patients needed immediate endotracheal intubation. Intubation was delayed in 44% of patients; in these patients, an initial attempt at noninvasive ventilation had failed. To make the decision of whether to intubate as objective as possible, we established criteria extrapolated from the study by Brochard and coworkers (9). Major criteria for intubation were respiratory arrest, loss of consciousness, psychomotor agitation requiring sedation, hemodynamic instability with systolic blood pressure less than 70 mm Hg or greater than 180 mm Hg, and a heart rate of 50 beats/min or less with loss of alertness. Minor criteria were a respiratory rate that was more than 35 breaths/min and was higher than the value recorded on admission, an arterial $\text{pH}$ that was 7.30 or less and was lower than the value recorded on admission, a $\text{PaO}_2$ less than 45 mm Hg despite oxygen supplementation, deterioration of one or more points in the neurologic score of the scale of Kelly and Matthay (17), and presence of a weak cough reflex with accumulation of secretions. The presence of one major criterion was considered an indication for immediate intubation. In patients undergoing an initial attempt at noninvasive ventilation, the presence of two minor criteria after 1 hour of treatment or less was considered to indicate the need for intubation.

Patients were excluded from the study if they had concomitant severe diseases, such as neurologic diseases other than hypercapnic encephalopathy; cancer and other systemic diseases; cardiac arrest; cardiogenic pulmonary edema; cardiogenic shock; aortic aneurysm; acute myocardial infarction; gastrointestinal perforation, obstruction, or bleeding; sepsis; trauma; metabolic coma; diabetic ketoacidosis; drug overdose; coagulopathy; and other hematologic diseases. Postoperative patients were also excluded.

Patients were prospectively recruited from three hospitals in Montescano, Gussago, and Novi Ligure, Italy. Of the 68 patients referred to the participating centers and intubated for acute respiratory failure, 50 (74%) were enrolled. Eighteen patients were excluded at the time of possible randomization: Eight (12%) had a successful T-piece weaning trial at the time of randomization, 6 (9%) had altered neurologic status, and 4 (6%) were hemodynamically unstable.

The protocol was approved by each hospital's ethics committee. Patients or their relatives gave informed consent to the study.

Study Protocol

Intubation was done via the orotracheal route. After intubation, all patients were ventilated in controlled mode with intensive care unit ventilators for the first 12 hours; during the first 6 to 8 hours, the patients were sedated and curarized and their airway secretions were suctioned frequently. Standard settings for controlled ventilation were used: tidal volume, approximately 8 to 10 mL/kg; respiratory rate, 12 to 16 breaths/min; and an inspired oxygen fraction ($\text{FiO}_2$) as required to obtain an $\text{SaO}_2$ of about 95% ($41\% \pm 0.05\%$). Patients were then given pressure support ventilation ($21 \pm 2 \text{ cm H}_2\text{O}$) for an additional 24 to 36 hours. Extrinsic positive end-expiratory pressure was added when intrinsic positive end-expiratory pressure was clinically suspected. At the end of this brief period of invasive ventilation, a T-piece weaning trial was carried out in patients who were judged to have reached satisfactory neurologic status, had a body temperature of 37°C or less, were hemodynamically stable, and had an $\text{SaO}_2$ of 88% or more for an $\text{FiO}_2$ of 40% during a brief discontinuation of mechanical ventilation.

We considered the T-piece trial to have failed if patients had any of the following: a respiratory rate more than 35 breaths/min, a $\text{PaO}_2$ less than 50 mm Hg for an $\text{FiO}_2$ of 40%, heart rate more than 145 beats/min or sustained increase or decrease in the heart rate of more than 20%, severe arrhythmia, systolic blood pressure more than 180 mm Hg or less than 70 mm Hg, agitation, anxiety, or diaphoresis. Patients in whom the weaning trial failed and who did not meet any of the aforementioned exclusion criteria were randomly assigned to receive noninvasive ventilation or to continue the weaning process with invasive pressure support ventilation.

The study was designed to enroll all eligible patients over a specified 18-month period. Random assignment was done by using opaque, sealed, numbered envelopes. A post hoc analysis was performed to confirm the validity of the randomization. To detect any possible differences in the two groups at enrollment, the 50 patients were divided according...
to the random assignments, survival or death, and successful and unsuccessful weaning.

Immediately after failure of the T-piece weaning trial, patients were reconnected to the ventilator in pressure support ventilation mode until the previous $\text{PaCO}_2$ and pH values were reached (30 to 60 minutes) and the respiratory rate under ventilation was 30 breaths/min or less. Patients in the noninvasive ventilation group were then extubated and switched to noninvasive pressure support ventilation with a face mask (Gibeck Respiration AB, Upplands-Vasby, Sweden) and the same ventilator. The patients' heart rate, electrocardiograms, $\text{SaO}_2$, and blood pressure were monitored continuously, and a physician was present to intubate patients again, if necessary. Patients received ventilation with a level of pressure support ($19 \pm 2 \text{ cm H}_2\text{O}$) that was adjusted to achieve satisfactory blood gases and a respiratory rate of less than 25 breaths/min. During the first 48 hours after extubation, noninvasive ventilation was delivered until it was well tolerated (20 to 22 hours per day), spaced by periods of spontaneous inhalation of oxygen only during meals and to expectorate.

The level of pressure support was decreased by 2 or 4 cm H$_2$O per day in patients with good tolerance; patients were allowed to breathe spontaneously. At least two trials of spontaneous breathing of gradually increased duration were attempted each day.

To assess weaning from noninvasive ventilation as objectively as possible, the following criteria recorded after at least 3 hours of spontaneous breathing were established: $\text{SaO}_2$ of 90% or more with an $\text{FiO}_2$ of 40% or less, pH of 7.35 or more, respiratory rate less than 35 breaths/min, hemodynamic stability, absence of severe dyspnea, and depressed neurologic status. The absence of even one of these criteria was considered failure to wean, and the patient was reconnected to the ventilator (which was always set at its maximal trigger sensitivity). Weaning was considered successful if reintubation or noninvasive ventilation was not required within 72 hours of suspension of ventilation.

In intubated patients who received pressure support ventilation, the pressure was titrated to achieve a breathing frequency of 25 breaths/min or less. Pressure support ventilation was initially set at $17.6 \pm 2.1 \text{ cm H}_2\text{O}$. For patients who received invasive ventilation, the level of pressure support was gradually decreased and intermittent trials of spontaneous breathing were performed twice a day by using a T-tube circuit or a continuous-flow circuit with a continuous positive airway pressure of less than 5 cm H$_2$O (4). The weaning criteria were the same as those used for noninvasive ventilation.

Arterial blood gases were collected from the radial artery (ABL 300, Radiometer, Copenhagen, Denmark) at admission; 1, 4, 8, and 12 hours after the beginning of each ventilatory treatment; and after changes in the ventilatory setting. The neurologic score was recorded once daily. Pulmonary function tests were performed with a portable spirometer as soon as the patients' clinical condition allowed testing and before discharge from the intensive care unit in all cases.

Ventilator-associated pneumonia was defined as the presence, during mechanical ventilation, of a new and persistent (>48 hours) lung infiltrate on chest radiography combined with at least two of the following conditions: fever, peripheral leukocyte count higher than 10 000 cells/mm$^3$, and endotracheal secretion obtained by suctioning material from the lower respiratory tract in which a Gram stain showed one or more types of bacteria.

**Statistical Analysis**

Results are given as the mean ± SD. All statistical tests were two-sided. Groups were compared by using unpaired or paired t-tests as appropriate when normality assumptions were satisfied and by using the Mann–Whitney test and Wilcoxon test when normality assumptions were not satisfied. Frequency distributions were compared by using the chi-square test. Multiple comparisons were done with an analysis of variance for repeated measures; if necessary, post hoc analysis was corrected by using the Bonferroni test. The Kaplan–Meier estimate-of-survival curve was used to determine the probability of success of the two methods over time and the survival rate at 60 days; survival curves were compared by using the log-rank test. Treatment was considered to have failed if 1) the patient could not be taken off of the ventilator after 60 days (this cut-off was chosen because patients with chronic obstructive pulmonary disease have been shown to have longer weaning times than patients with other conditions (18–22), 2) endotracheal reintubation was required within 72 hours after disconnection from the ventilator, or 3) death related to mechanical ventilation occurred. Nosocomial pneumonia, pneumothorax, ischemic cardiac events, or fatal arrhythmia during the weaning process were causes of death considered to be associated with mechanical ventilation (3). A P value less than 0.05 was considered statistically significant.

**Role of Funding Source**

Our study did not receive any financial support.
Table 1. Physiologic Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Noninvasive Pressure Support Ventilation Group</th>
<th>Invasive Pressure Support Ventilation Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68.7 ± 8.5</td>
<td>67.0 ± 9.2</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>24.3 ± 3.1</td>
<td>23.1 ± 4.5</td>
</tr>
<tr>
<td>Leukocyte count, cells/mm³</td>
<td>8488 ± 1345</td>
<td>8112 ± 1789</td>
</tr>
<tr>
<td>Albumin level, g/dL</td>
<td>34.0 ± 10.0</td>
<td>36.0 ± 7.0</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>32.7 ± 8.7</td>
<td>30.6 ± 7.1</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>101 ± 12</td>
<td>106 ± 11</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>133 ± 28</td>
<td>139 ± 22</td>
</tr>
<tr>
<td>pH</td>
<td>7.22 ± 0.07</td>
<td>7.22 ± 0.08</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
<td>96.3 ± 19.6</td>
<td>91.9 ± 13.6</td>
</tr>
<tr>
<td>PaCO₂/PaO₂ ratio</td>
<td>1.48 ± 0.3</td>
<td>1.42 ± 0.4</td>
</tr>
<tr>
<td>FEV₁, mL</td>
<td>501 ± 131</td>
<td>525 ± 129</td>
</tr>
<tr>
<td>Percent predicted FEV₁</td>
<td>16.9 ± 10</td>
<td>17.4 ± 9</td>
</tr>
<tr>
<td>Vital capacity, mL</td>
<td>592 ± 208</td>
<td>1089 ± 222</td>
</tr>
<tr>
<td>Percent predicted vital capacity</td>
<td>26.0 ± 8</td>
<td>29.2 ± 9</td>
</tr>
</tbody>
</table>

* Data are the mean ± SD. APACHE = Acute Physiology, Age, and Chronic Health Evaluation; Fio₂ = fraction of inspired oxygen.
† See reference 17.
‡ Data are given for 14 patients in the noninvasive ventilation group and 16 patients in the invasive ventilation group.

Results

Patients

Twenty-five patients were randomly assigned to be extubated and to undergo the weaning process with noninvasive pressure support ventilation, and 25 remained intubated and received the same mode of ventilation. Of the 50 patients, 26 were enrolled in Montescano (14 in the group that received noninvasive ventilation [1 death] and 12 in the group that received invasive ventilation [4 deaths]), 14 were enrolled in Novi Ligure (6 in the group that received noninvasive ventilation [1 death] and 8 in the group that received invasive ventilation [2 deaths]), and 10 were enrolled in Gussago (5 in the group that received noninvasive ventilation [no deaths] and 5 in the group that received invasive ventilation [1 death]).

As shown in Tables 1 and 2, the two groups of patients had similar functional and clinical characteristics at admission. Comorbid conditions were present in 14 patients who received noninvasive ventilation and 11 patients who received invasive ventilation. In the noninvasive ventilation group, 5 patients had hypertension, 4 had rhythm disturbances, 3 had congestive heart failure, 3 had diabetes, 2 had sepsis of the urinary tract, and 1 had diverticulosis. Four patients had two of the aforementioned conditions. In the invasive ventilation group, 4 patients had hypertension, 4 had rhythm disturbances, 3 had congestive heart failure, 1 had diabetes, and 1 had hepatic failure. Two patients had two of the aforementioned conditions. At the time of hospital admission, most patients (35 of 50) were receiving long-term oxygen therapy; 18 of these patients were randomly assigned to noninvasive ventilation (10 in Montescano, 4 in Novi Ligure, and 4 in Gussago), and 17 were assigned to continue invasive ventilation (9 in Montescano, 5 in Novi Ligure, and 3 in Gussago). Patients were also receiving standard therapy for chronic obstructive pulmonary disease, including β₂-agonists (42 patients), theophylline (21 patients), anticholinergic agents (13 patients), and diuretics (13 patients).

The results of post hoc analysis did not show any significant differences in the two groups at admission (Tables 1 and 2) or at randomization (Table 3) for any of the physiologic variables or for the presence of comorbid conditions.

Outcomes

Figure 1 shows the changes in pH and PaCO₂ in the two groups of patients from the time of intubation to discharge from the intensive care unit. Institution of invasive ventilation significantly improved blood gas values (P < 0.001), which remained constant throughout the entire period of ventilation, regardless of the mode of ventilation. At discharge, these values were also similar during spontaneous breathing with oxygen supplementation.

Expiratory tidal volume per kilogram was similar in the two groups during mechanical ventilation, regardless of the level of pressure support applied (mechanical ventilation immediately after randomization, 8.4 ± 0.5 mL/kg with pressure support of 19.0 ± 2.0 cm H₂O for the noninvasive ventilation group and 8.2 ± 0.3 mL/kg with pressure support of

Table 2. Location before the Intensive Care Unit, Length of Hospital Stay, Number of Hospitalizations in the Previous Year, and Activity Limits because of Chronic Obstructive Pulmonary Disease*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Noninvasive Pressure Support Ventilation Group</th>
<th>Invasive Pressure Support Ventilation Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location before the intensive care unit</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Emergency department</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Other intensive care unit</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other hospital</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hospital floor</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Length of hospital stay before the intensive care unit</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>0 days</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>1 day</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2–4 days</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>5–10 days</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>11–30 days</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Functional limits because of chronic obstructive pulmonary disease</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Severe</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Hospitalizations in the previous year</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>0</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>1</td>
<td>11</td>
<td>10</td>
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<tr>
<td>2</td>
<td>6</td>
<td>7</td>
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<tr>
<td>&gt;2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Location before the Intensive Care Unit, Length of Hospital Stay, Number of Hospitalizations in the Previous Year, and Activity Limits because of Blockchain Pulmonary Disease*
17.6 ± 2.0 cm H₂O for the invasive ventilation group; 50% of the ventilatory time, 8.2 ± 0.4 mL/kg with pressure support of 16.1 ± 1.6 cm H₂O for the noninvasive ventilation group and 8.1 ± 0.3 mL/kg with pressure support of 15.2 ± 1.3 cm H₂O for the invasive ventilation group; and just before successful weaning, 8.3 ± 0.3 mL/kg with pressure support of 9.7 ± 0.5 cm H₂O for the noninvasive ventilation group and 8.1 ± 0.4 mL/kg with pressure support of 9.3 ± 0.3 cm H₂O for the invasive ventilation group). The minute of ventilation per kilogram also remained similar for both groups (mechanical ventilation immediately after randomization, 198.1 ± 8.3 mL/kg per minute for the noninvasive ventilation group and 188.8 ± 24.9 mL/kg per minute for the invasive ventilation group; 50% of the ventilatory time, 164.3 ± 21.8 mL/kg per minute for the noninvasive ventilation group and 152.8 ± 18.0 mL/kg per minute for the invasive ventilation group; and just before successful weaning, 124.5 ± 18.3 mL/kg per minute in the noninvasive ventilation group and 119.9 ± 21.2 mL/kg per minute in the invasive ventilation group).

Some minor side effects were recorded in the noninvasive ventilation group. Twenty patients had cutaneous irritation of the nose; 14 of the 20 had nose abrasion, which was severe in some cases. Two patients had gastric distention, and most patients reported poor sleep, especially in the first few days.

Compared with patients who were weaned by using the invasive technique, patients who were weaned by using the noninvasive technique spent significantly fewer days receiving mechanical ventilation (15.6 ± 11.8 days and 10.2 ± 6.8 days; \( P = 0.021 \)) and in the intensive care unit (24.0 ± 13.7 days and 15.1 ± 5.4 days; \( P = 0.005 \)). Figure 2 shows the percentage of patients who could not be weaned (because of death associated with mechanical ventilation, reintubation within 72 hours, and failure to be weaned at 60 days) for the two methods of weaning. The failure rate among patients weaned with invasive pressure support ventilation was significantly higher than the rate among patients undergoing noninvasive ventilation \( (P = 0.002) \). Furthermore, at day 21 (the time point usually considered to be a threshold that separates weanable from unweanable patients [3]), the success rate was significantly higher in patients who received noninvasive treatment \( (P = 0.003) \).

Seven of 25 patients (28%) in the invasive ventilation group and no patients in the noninvasive ventilation group developed nosocomial pneumonia. The attack rate for pneumonia by ventilator day was one patient on day 3, two patients on day 5, one patient on day 7, one patient on day 8, one patient on day 16, and one patient on day 22.

Two of 25 patients (8%) in the noninvasive ventilation group died in the first 60 days. One patient in whom weaning attempts failed was discharged with a prescription for nasal ventilation to be given for 14 to 18 hours per day. Seven patients (28%) who were weaned by using invasive ventilation died; 2 were considered unweanable and were discharged with a prescription for at-home mechanical ventilation through a tracheostomy. The mortality rate at 60 days, assessed by using a mortality table, was significantly higher in the invasive ventilation group.
than in the noninvasive ventilation group (92% and 72%; P = 0.009).

Causes of death in the noninvasive ventilation group were multiple organ failure (1 patient on day 7) and myocardial infarction (1 patient on day 18). Fatal events in the invasive ventilation group were pneumonia (4 patients, one each on day 8, 10, 18, and 23), pneumothorax (1 patient on day 11), arrhythmia (1 patient on day 12), and pulmonary embolism (1 patient on day 21). One death in each group was not considered to be linked to mechanical ventilation (1 case of multiple organ failure and 1 case of pulmonary embolism).

At discharge from the intensive care unit, patients in the noninvasive ventilation group and the invasive ventilation group were similar for FEV1 (510 ± 111 mL or 17.1% ± 11.0% of the predicted value and 537 ± 92 mL or 17.8% ± 9.0% of the predicted value), vital capacity (901 ± 162 mL or 27.3% ± 10.0% of the predicted value and 937 ± 151 mL or 29.2% ± 12.0% of the predicted value), and the ratio of the two measures (56% ± 9% and 58% ± 11%).

Discussion

Our study shows that in patients with chronic obstructive pulmonary disease and acute respiratory failure, a new approach to ventilation that combines invasive ventilation for not more than 48 hours followed by noninvasive pressure support ventilation is more effective than pressure support ventilation delivered invasively for the entire ventilation period. With this approach, the intensive care unit stay is shorter, the incidence of nosocomial pneumonia is lower, and the survival rate at 60 days is higher.

The process of discontinuing mechanical ventilation constitutes a major clinical challenge, especially in patients with chronic obstructive pulmonary disease, in whom weaning is particularly difficult. The rate of weaning failure ranges from 35% to 67% according to various studies, the modes of ventilation used, and the definition of weaning (18-22). Noninvasive ventilation has been proposed as an alternative to intubation in the management of acute respiratory failure due to chronic obstructive pulmonary disease. Several studies (10, 23-25) have shown the efficacy of this method of ventilation in reducing the need for intubation; however, only a few studies were controlled and randomized (9, 26, 27). In their multicenter randomized study, Brochard and coworkers (9) found that noninvasive ventilation may avoid intubation, but only in selected patients; most patients (69%) in that study required immediate intubation for safety reasons. The reasons for needing immediate intubation or failure of noninvasive ventilation are mainly linked to hypercapnic-related nervous system disorders, such as neurologic depression; psychomotor agitation requiring sedation; weak cough reflex with difficulty in clearing the airways; and respiratory arrest, probably caused by acute fatigue of the respiratory muscles. In most of these patients, positioning of the endotracheal tube and short-term sedation or curarization allow prompt correction of acidosis and, consequently, improvement of the neurologic status, removal of secretions, and rest for the respiratory muscles. We undertook our study to assess the feasibility of substituting traditional invasive ventilation with the noninvasive technique at this point.

Few data are available on the use of noninvasive ventilation in the weaning process, and noninvasive ventilation has been applied only after a long period of invasive ventilation (11-13). For example, Restrick and associates (13) used noninvasive methods to wean patients with acute respiratory failure. The average time of invasive ventilation was long (40.9 days); of interest, two of their patients were successfully treated noninvasively only 24 hours after intubation. Our study validates these sporadic reports.

The main reason for the success of the noninvasive technique is probably that the technique avoids some of the most important complications of artificial airways. For example, the early institution of noninvasive ventilation was associated with a lower incidence of nosocomial pneumonia in our study. Torres and coworkers (5) considered the correlation between several risk factors and the development of nosocomial pneumonia; presence of chronic obstructive pulmonary disease and invasive ventilation...
for more than 3 days were significantly associated with an increased risk for nosocomial pneumonia. This finding has been confirmed by other investigators (6–8). An endotracheal tube can predispose to the development of pneumonia by impairing cough and mucociliary clearance because contaminated secretions can accumulate above the cuff and leak around the cuff or because bacterial binding to the surface of bronchial epithelium is increased. With a noninvasive ventilatory technique, the risk for aspiration of colonized or infected oropharyngeal secretions is probably smaller, there is no tracheal prosthesis, the patient can expectorate freely, and the vocal cords are not kept open.

Long-term invasive ventilatory support also increases the risk for feeding aspiration. Elpern and coworkers (28) showed that about 50% of tracheotomized patients receiving prolonged positive-pressure ventilation had feeding aspiration and that advanced age increased the risk for feeding aspiration. Ventilation delivered by a mask, on the other hand, enables patients to eat during spontaneous breathing periods, probably helping to avoid the risk for food aspiration.

The mortality rate at 60 days was significantly higher in patients treated only with invasive ventilation. The duration of exposure to mechanical ventilation and the different invasiveness of the two ventilatory modes may have influenced the outcome of these patients. Six of the seven deaths (86%) among the intubated patients were considered to have been linked to mechanical ventilation.

Despite the encouraging results of our study, it must be remembered that the study was conducted in a selected group of severely hypercapnic patients with chronic obstructive pulmonary disease. Extubation was done only if patients reached a satisfactory neurologic status, a body temperature of 37°C or less, hemodynamic stability, and $\text{SaO}_2$ of 88% or more for an $\text{FiO}_2$ of 40%. This new weaning technique may not be applicable to patients who are sicker, have more severe comorbid conditions, or are affected by severe hypoxemic respiratory failure. Another potential problem related to the use of noninvasive ventilation is the fact that it may be an excessively time-consuming procedure for medical and paramedical staff (29). Although this may be true in the first 2 days of ventilation, it has been recently shown that after this time, the human resources needed are significantly less in patients receiving noninvasive ventilation than in patients undergoing invasive ventilation (30).

In conclusion, in a selected population of patients with severe hypercapnic acute respiratory failure who needed prompt intubation, early extubation and application of pressure support ventilation by a noninvasive route as a bridge to weaning reduced the duration of mechanical ventilation, the duration of intensive care unit stay, and the occurrence of nosocomial pneumonia and was associated with a better 60-day survival rate than was the same treatment delivered invasively. However, further studies are needed to assess the clinical efficacy of this technique in patients who are sicker or who have pure hypoxemic respiratory failure.

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More thorough and scientific medicines employed, even equally free of charge, by doctors of the first reputation, would not have brought nearly so many poor people together and, above all, would not have done them so much good. There would have been lacking the main instruments of healing—prevention, respect, faith, and gratitude. Man is composed of a soul and a body and it is the former that governs the latter. The wounded who have received consolation, the sick who have been persuaded to hope are already in a state to be cured; their blood circulates better, their nerves are strengthened, sleep returns, and the body revives. Nothing is more efficacious than confidence.

Duff Cooper
Talleyrand

Submitted by:
Henryk Kafka, MD, FRCP
Belleville, Ontario, Canada

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