

## A COMPARISON OF NONINVASIVE POSITIVE-PRESSURE VENTILATION AND CONVENTIONAL MECHANICAL VENTILATION IN PATIENTS WITH ACUTE RESPIRATORY FAILURE

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### ABSTRACT

**Background and Methods** The role of noninvasive positive-pressure ventilation delivered through a face mask in patients with acute respiratory failure is uncertain. We conducted a prospective, randomized trial of noninvasive positive-pressure ventilation as compared with endotracheal intubation with conventional mechanical ventilation in 64 patients with hypoxemic acute respiratory failure who required mechanical ventilation.

**Results** Within the first hour of ventilation, 20 of 32 patients (62 percent) in the noninvasive-ventilation group and 15 of 32 (47 percent) in the conventional-ventilation group had an improved ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ( $\text{PaO}_2:\text{FiO}_2$ ) ( $P=0.21$ ). Ten patients in the noninvasive-ventilation group subsequently required endotracheal intubation. Seventeen patients in the conventional-ventilation group (53 percent) and 23 in the noninvasive-ventilation group (72 percent) survived their stay in the intensive care unit (odds ratio, 0.4; 95 percent confidence interval, 0.1 to 1.4;  $P=0.19$ ); 16 patients in the conventional-ventilation group and 22 patients in the noninvasive-ventilation group were discharged from the hospital. More patients in the conventional-ventilation group had serious complications (66 percent vs. 38 percent,  $P=0.02$ ) and had pneumonia or sinusitis related to the endotracheal tube (31 percent vs. 3 percent,  $P=0.003$ ). Among the survivors, patients in the noninvasive-ventilation group had shorter periods of ventilation ( $P=0.006$ ) and shorter stays in the intensive care unit ( $P=0.002$ ).

**Conclusions** In patients with acute respiratory failure, noninvasive ventilation was as effective as conventional ventilation in improving gas exchange and was associated with fewer serious complications and shorter stays in the intensive care unit. (N Engl J Med 1998;339:429-35.)

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**N**ONINVASIVE positive-pressure ventilation is a safe and effective means of improving gas exchange in patients with many types of acute respiratory failure.<sup>1</sup> For example, in patients with acute exacerbations of chronic obstructive pulmonary disease and hypercapnic respiratory failure, adding noninvasive ventilation to standard therapy decreased the need for endotracheal intubation<sup>2-9</sup> and reduced mortality.<sup>8</sup> Similarly,

noninvasive continuous positive airway pressure was effective in patients with cardiogenic pulmonary edema, particularly those with hypercapnia.<sup>10-12</sup> In patients with various forms of acute hypoxemic respiratory failure (pneumonia, congestive heart failure, chest-wall impairment, and so forth),<sup>6,13</sup> this therapy slightly decreased the rate of intubation and improved survival, but the effect was not statistically significant.<sup>8</sup> The efficacy of positive-pressure ventilation in patients with hypoxemic respiratory failure is not known.

We compared the efficacy of noninvasive ventilation delivered through a face mask with the efficacy of conventional mechanical ventilation delivered through an endotracheal tube in patients with severe hypoxemia whose condition had not improved with aggressive medical therapy and who required mechanical ventilation.

### METHODS

#### Study Design and Patient Selection

We enrolled consecutive adults with acute hypoxemic respiratory failure who were admitted to the intensive care unit of La Sapienza University Hospital in Rome. The patients were randomly assigned to receive either conventional mechanical ventilation with endotracheal intubation or noninvasive ventilation through a face mask. An ad hoc ethics committee approved the protocol, and all patients or their next of kin gave written informed consent.

The criteria for eligibility were acute respiratory distress that had deteriorated despite aggressive medical management, including severe dyspnea at rest as determined by a clinician who was not an investigator; a respiratory rate greater than 35 breaths per minute; a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ( $\text{PaO}_2:\text{FiO}_2$ ) of less than 200 while the patient was breathing oxygen through a Venturi mask; and active contraction of the accessory muscles of respiration or paradoxical abdominal motion. Patients with any of the following were excluded: chronic obstructive pulmonary disease according to previously defined criteria<sup>5</sup>; immunosuppressive therapy; a requirement of emergency intubation for cardiopulmonary resuscitation, respiratory arrest, severe hemodynamic instability, or encephalopathy; respiratory failure caused by neurologic disease or status asthmaticus; more than two new organ failures (e.g., the simultaneous presence of renal and cardiovascular failure)<sup>14</sup>; and

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tracheostomy, facial deformities, or recent oral, esophageal, or gastric surgery.

Medical management for the conditions causing acute respiratory failure was similar in the two groups. We used two types of mechanical ventilators: the Puritan Bennett 7200 (Puritan Bennett, Overland Park, Kans.) and the Servo 900 C (Siemens Elema, Uppsala, Sweden). The patients underwent continuous electrocardiography and monitoring of arterial oxygen saturation (Biox 3700, Ohmeda, Boulder, Colo.).

### Conventional Ventilation

Patients assigned to the conventional-ventilation group underwent intubation with cuffed endotracheal tubes (internal diameter, 7.5 to 8.5 mm). The initial ventilator setting was in the assist-control mode, with a delivered tidal volume of 10 ml per kilogram of body weight and a respiratory rate of 14 to 18 breaths per minute, a positive end-expiratory pressure of 5 cm of water, and an  $\text{FiO}_2$  of 0.8. Positive end-expiratory pressure was increased in increments of 2 to 3 cm of water up to 10 cm of water, until the  $\text{FiO}_2$  requirement was 0.6 or less. Intravenous diazepam (0.2 mg per kilogram) or propofol (2 mg per kilogram) was given for sedation at the time of intubation; none of the patients received a paralyzing drug. The head of the bed was kept elevated at an angle of 45 degrees to minimize the risk of aspiration. When spontaneous breathing reappeared, the ventilator settings were changed to intermittent mandatory ventilation (rate, 4 to 7 breaths per minute) with pressure support (14 to 20 cm of water), adjusted to achieve a spontaneous tidal volume of 8 to 10 ml per kilogram, a respiratory rate of fewer than 25 breaths per minute, and the disappearance of accessory-muscle activity.<sup>15</sup> All patients were weaned from the ventilator by reducing the level of pressure support by 4 cm of water twice and then decreasing the ventilatory rate by two breaths per minute at two-hour intervals, as tolerated. Patients who tolerated an intermittent-mandatory-ventilation rate of 0.5 breath per minute, a pressure-support level of 8 cm of water, and an  $\text{FiO}_2$  of 0.5 or less had a two-hour T-piece trial.<sup>16</sup> These patients then underwent extubation if they maintained a respiratory rate lower than 30 breaths per minute and a  $\text{PaO}_2$  greater than 75 mm Hg.

### Noninvasive Ventilation

For patients assigned to noninvasive ventilation, the ventilator was connected with soft-tubing to a clear, full-face mask with an inflatable soft-cushion seal and a disposable foam spacer to reduce dead space (Gibeck, Upplands, Sweden). The mask was secured with head straps to avoid an excessively tight fit, and the head of the bed was kept elevated at a 45-degree angle. In most cases, a hydrocolloid sheet was applied over the nasal bridge. For patients with a nasogastric tube, a seal connector in the dome of the mask was used to minimize air leakage. After the mask had been secured, pressure support was increased to achieve an exhaled tidal volume of 8 to 10 ml per kilogram, a respiratory rate of fewer than 25 breaths per minute, the disappearance of accessory-muscle activity (as evaluated by palpation of the sternocleidomastoid muscle),<sup>15</sup> and patient comfort. Continuous positive airway pressure was increased by 2 to 3 cm of water repeatedly, up to 10 cm of water, until the  $\text{FiO}_2$  requirement was 0.6 or less. Ventilator settings were adjusted on the basis of continuous oximetry and measurements of arterial-blood gases. The patients were not sedated.

The duration of ventilation was standardized according to the protocol of Wysocki et al.<sup>13</sup> During the first 24 hours, ventilation was continuously maintained until oxygenation and clinical status improved. Subsequently, each patient was evaluated daily after breathing supplemental oxygen without ventilatory support for 15 minutes. Noninvasive ventilation was reduced progressively in accordance with the degree of clinical improvement and was discontinued if the patient maintained a respiratory rate lower than 30 breaths per minute and a  $\text{PaO}_2$  greater than 75 mm Hg with an  $\text{FiO}_2$  of 0.5, without ventilatory support.

In the patients randomly assigned to receive noninvasive ventilation, the criteria for switching them to endotracheal intubation and conventional ventilation were the failure to maintain a  $\text{PaO}_2$  above 65 mm Hg with an  $\text{FiO}_2$  of at least 0.6; the development of conditions necessitating endotracheal intubation to protect the airways (coma or seizure disorder) or to manage copious tracheal secretions; hemodynamic or electrocardiographic instability; or an inability on the part of the patient to tolerate the face mask because of discomfort. An attending physician who was not an investigator evaluated these criteria.

### End Points and Definitions

The primary end points were the values for gas exchange and the frequency of complications of mechanical ventilation, including pneumonia, sepsis, and sinusitis. Arterial-blood gas values were determined at base line, at one hour, at four-hour intervals during mechanical ventilation, and before discontinuation of ventilatory support. Improvement in gas exchange was defined as the ability to increase the  $\text{PaO}_2$ : $\text{FiO}_2$  ratio to more than 200 or an increase in this ratio of more than 100 from base line.<sup>12</sup> Improvement in gas exchange was evaluated within one hour after study entry (initial improvement) and over time (sustained improvement). Sustained improvement in gas exchange was defined as the ability to maintain the defined improvement in  $\text{PaO}_2$ : $\text{FiO}_2$  until mechanical ventilation was discontinued, as confirmed by serial blood gas measurements.

Patients were monitored for the development of infections or other complications. Sepsis was defined as a systemic inflammatory response to an infectious process, with manifestations including tachycardia, tachypnea, hyperthermia, and hypothermia, and a high white-cell count; positive blood cultures were not required. Severe sepsis was diagnosed when sepsis was associated with evidence of organ dysfunction or hypoperfusion, such as altered mental status, metabolic acidosis, or oliguria. Severe sepsis associated with hypotension that was unresponsive to fluid therapy was referred to as septic shock.<sup>17</sup>

Patients in whom clinical manifestations of pneumonia developed, including radiographic evidence of persistent pulmonary infiltrates, hyperthermia or hypothermia, purulent tracheobronchial secretions, a high white-cell count, and worsening of pulmonary-gas exchange,<sup>18,19</sup> underwent bronchoscopy with bronchoalveolar lavage. The methods and laboratory procedures followed consensus guidelines.<sup>20,21</sup> Pneumonia was diagnosed when at least 100,000 colony-forming units of bacteria per milliliter were measured in bronchoalveolar-lavage fluids.<sup>20</sup> Since infections in patients receiving mechanical ventilation are frequently associated with the presence of an invasive device,<sup>18</sup> an index of invasiveness was established by counting the number of devices (central venous, arterial, pulmonary arterial, and urinary catheters; drainage, endotracheal, and nasogastric tubes) per patient at entry to the study.

The secondary end points were survival, the duration of mechanical ventilation, and the duration of the stay in the intensive care unit. The criteria for the diagnosis of the acute respiratory distress syndrome were those of the American-European Consensus Conference.<sup>22</sup> The simplified acute physiologic score was calculated 24 hours after admission to the intensive care unit.<sup>23</sup> This score takes into account 14 variables (age, heart rate, systolic blood pressure, body temperature, respiratory rate or need for ventilatory support, urinary output, white-cell count, hematocrit, Glasgow coma score, and serum glucose, potassium, sodium, bicarbonate, and urea nitrogen concentrations). A range of 0 to 4 is assigned for each variable (range of possible scores, 0 to 56). Higher scores indicate a higher risk of death; for instance, a score of 15 or 16 is associated with a mortality rate of approximately 32 percent, and for all scores of 21 or higher, mortality exceeds 80 percent.

### Statistical Analysis

Results are given as means  $\pm$ SD. Demographic and physiologic characteristics of the two groups were compared with use of Stu-

dent's t-test for continuous data (separate estimates of variance were used when variances differed significantly) and with the Mantel-Haenszel extended chi-square test for categorical data. Fisher's exact test (two-tailed) was used when appropriate (when the expected number of cases per cell was below five). The SPSS package (SPSS, Chicago) was used for all analyses. The odds ratios, relative risks, and 95 percent confidence intervals are given with chi-square and P values to illustrate the amount of risk associated with some of the effects.<sup>24</sup>

## RESULTS

Between April 1995 and March 1996, 486 patients were admitted to the intensive care unit; 295 had already undergone intubation, 19 underwent tracheostomy, and 95 had chronic obstructive pulmonary disease or were receiving immunosuppressive therapy. Of the 77 patients who met the entry criteria, 13 chose not to participate; thus, 64 were enrolled. Thirty-two patients were assigned to each group. The base-line characteristics of the two groups were similar (Table 1), with the exception that in the conventional-ventilation group the mean arterial pH was significantly lower ( $P=0.002$ ) and more patients had a partial pressure of arterial carbon dioxide ( $\text{PaCO}_2$ ) greater than 45 mm Hg (12 vs. 5 patients,  $P=0.05$ ). The treatments for the conditions precipitating respiratory failure and the ventilatory requirements were similar. The mean level of applied positive end-expiratory pressure was similar ( $5.1 \pm 1.4$  cm of water in the noninvasive-ventilation group and  $5.3 \pm 1.2$  cm of water in the conventional-ventilation group).

The patients in the two groups had a similar initial change in  $\text{PaO}_2:\text{FiO}_2$  (Fig. 1). Within the first hour of mechanical ventilation, 20 patients (62 percent) in the noninvasive-ventilation group and 15 (47 percent) in the conventional-ventilation group had an improvement in  $\text{PaO}_2:\text{FiO}_2$  ( $P=0.21$ ). The  $\text{PaO}_2:\text{FiO}_2$  improved over time in the 22 patients in the noninvasive-ventilation group who did not need intubation ( $116 \pm 25$  at base line vs.  $250 \pm 60$  at the end of treatment,  $P=0.02$ ) and in the 17 patients in the conventional-ventilation group who survived ( $126 \pm 25$  at base line vs.  $241 \pm 98$  at the end of treatment,  $P=0.03$ ). The change in  $\text{PaCO}_2$  was similar in the two groups. Ten patients in the noninvasive-ventilation group (31 percent) required endotracheal intubation an average of  $15 \pm 7$  hours after entry into the study, but none required emergency intubation. The reasons for intubation were the failure of noninvasive ventilation to maintain the  $\text{PaO}_2$  above 65 mm Hg (four patients), its inability to correct dyspnea (one patient), its inability to manage copious secretions (one patient), intolerance of noninvasive ventilation (two patients), and hemodynamic instability (two patients).

Overall, 42 patients, including 10 in the noninvasive-ventilation group, underwent intubation; 14 had orotracheal intubation, and 28 had nasotracheal intubation. The length of stay in the intensive care

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS AND CAUSES OF ACUTE RESPIRATORY FAILURE.\*

VARIABLE†	NONINVASIVE-VENTILATION GROUP (N=32)	CONVENTIONAL-VENTILATION GROUP (N=32)
Patients' characteristics		
Age — yr	52±19	57±18
Male sex — no. (%)	18 (56)	20 (62)
SAPS	13±4	12±4
Heart rate — beats/min	100±21	110±17
Respiratory rate — breaths/min	39±4	39±5
Body temperature — °C	36.8±0.7	36.8±0.6
Systolic blood pressure — mm Hg	135±28	132±29
Arterial pH‡	7.45±0.1	7.37±0.1
$\text{PaCO}_2$ — mm Hg	38±9	42±11
$\text{PaCO}_2 > 45$ mm Hg — no. (%)§	5 (16)	12 (38)
$\text{PaO}_2:\text{FiO}_2$	116±24	124±25
Causes of acute respiratory failure — no. (%)		
Pneumonia	5 (16)	4 (12)
Trauma	4 (12)	4 (12)
Cardiogenic pulmonary edema	7 (22)	5 (16)
Postoperative respiratory failure¶		
Acute respiratory distress syndrome	7 (22)	9 (28)
Mucous plugging or atelectasis	7 (22)	9 (28)
Gastric contents aspiration without acute respiratory distress syndrome	2 (6)	1 (3)

\*Plus-minus values are means ±SD.

†SAPS denotes simplified acute physiologic score, which is explained in detail in the Methods section.<sup>23</sup> The range of possible values is 0 to 56; higher scores indicate a higher risk of death.  $\text{PaCO}_2$  denotes the partial pressure of arterial carbon dioxide, and  $\text{PaO}_2:\text{FiO}_2$  the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen.

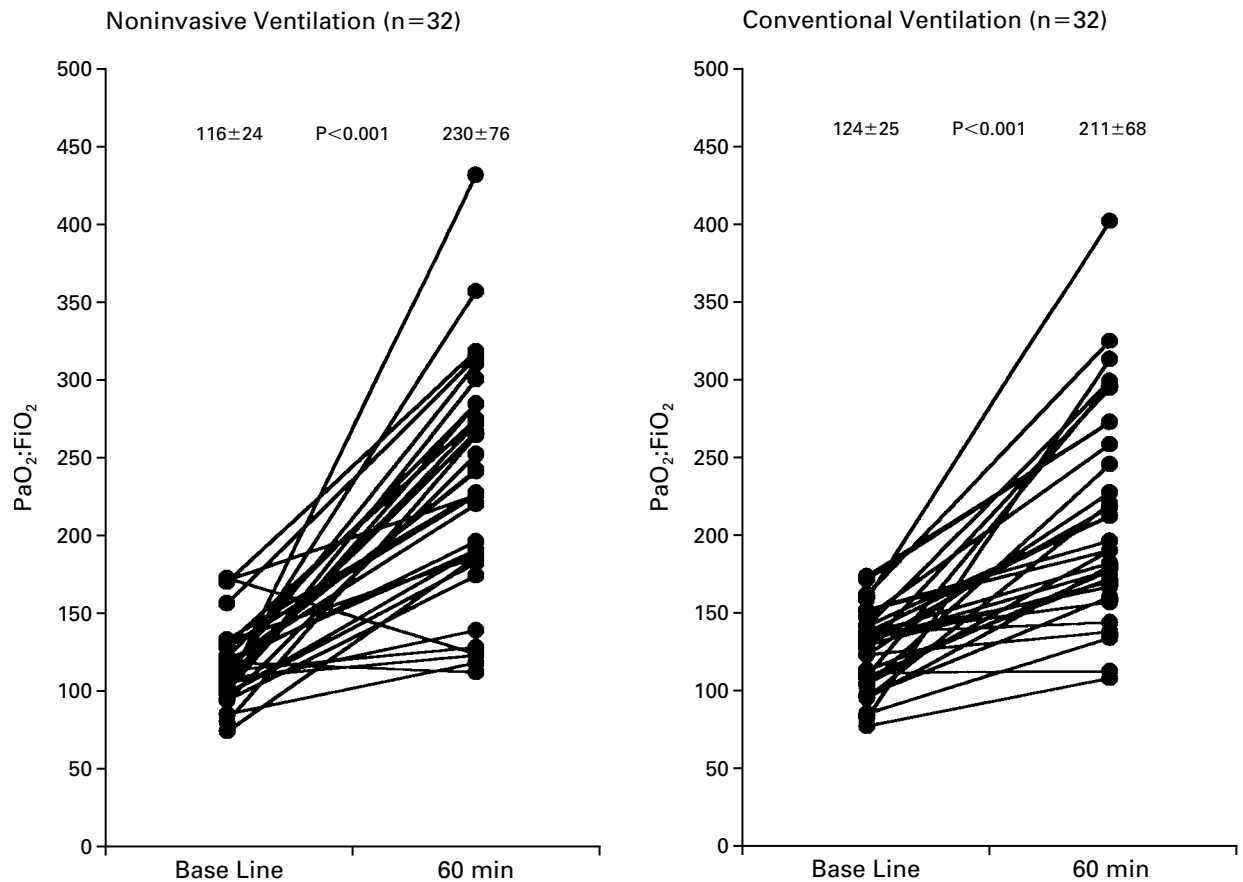
‡ $P=0.002$  for the comparison between the groups.

§ $P=0.05$  for the comparison between the groups.

¶The types of operations in the noninvasive-ventilation and conventional-ventilation groups, respectively, included major vascular operations (five and four patients), colorectal operations (four and six patients), genitourinary-obstetrical operations (three and five patients), orthopedic operations (two patients in each group), and thoracic operations (two patients in each group).

||The conditions of the acute respiratory distress syndrome in the noninvasive-ventilation and conventional-ventilation groups, respectively, included aspiration of gastric contents (two and four patients), fat embolism (one patient in each group), pancreatitis (one patient in each group), sepsis (two patients and none), and massive blood transfusion (one and three patients).

unit was shorter for patients in the noninvasive-ventilation group ( $9 \pm 7$  days, vs.  $16 \pm 17$  days in the conventional-ventilation group;  $P=0.04$ ). Nine patients in the noninvasive-ventilation group — all of whom required endotracheal intubation — and 15 in the conventional-ventilation group died in the intensive care unit. Thus, the rate of survival to discharge from the intensive care unit was 53 percent (17 patients) in the conventional-ventilation group and 72 percent (23 patients) in the noninvasive-ventilation group (odds ratio, 0.4; 95 percent confidence interval, 0.1 to 1.4;  $P=0.19$ ). Two patients (one in each group) died in the hospital after discharge from intensive care. One, in the noninvasive-ventilation group, died of ventricular fibrillation. The other, in the conven-



**Figure 1.** The Ratio of the Partial Pressure of Arterial Oxygen to the Fraction of Inspired Oxygen ( $\text{PaO}_2:\text{FiO}_2$ ) at Base Line and after One Hour of Mechanical Ventilation in Patients with Acute Respiratory Failure in the Noninvasive-Ventilation and Conventional-Ventilation Groups.

A paired t-test was used for the statistical comparison. The degree of improvement in gas exchange after the start of mechanical ventilation was similar in the two groups. The values shown within the panels are means  $\pm$ SD.

tional-ventilation group, died of cardiogenic shock due to a new myocardial infarction. The other patients were successfully discharged from the hospital without further complications.

The complications and events leading to death are shown in Table 2. More patients in the conventional-ventilation group than in the noninvasive-ventilation group had serious complications (66 percent vs. 38 percent,  $P=0.02$ ) and had pneumonia or sinusitis related to the endotracheal tube (31 percent vs. 3 percent,  $P=0.003$ ). The rate of serious complications was higher in patients in the conventional-ventilation group. Among the patients in the noninvasive-ventilation group, 12 (38 percent) had serious complications after undergoing endotracheal intubation. One of the 12 patients in whom noninvasive ventilation failed had pneumonia diagnosed six days after undergoing endotracheal intubation.

Further details of patient outcomes are shown in Table 3. In the noninvasive-ventilation group, there was a sustained improvement in gas exchange over

time in 17 of the 22 patients who did not undergo intubation but in only 2 of the 10 patients who required intubation ( $P=0.003$ ). Avoiding intubation was associated with a lower incidence of septic complications ( $P=0.006$ ). Among the 40 patients who survived to be discharged from the intensive care unit, the patients in the noninvasive-ventilation group had a shorter duration of mechanical ventilation ( $3\pm 3$  vs.  $6\pm 5$  days,  $P=0.006$ ) and a shorter stay in the intensive care unit ( $6.6\pm 5$  vs.  $14\pm 13$  days,  $P=0.002$ ) than those in the conventional-ventilation group.

Among the patients in the conventional-ventilation group, those who died had a higher simplified acute physiologic score ( $P=0.02$ ). A post hoc subgroup analysis was performed for patients with simplified acute physiologic scores lower than 16 and for those with scores of at least 16. The 19 patients with simplified acute physiologic scores of at least 16 had similar outcomes regardless of the type of ventilation, whereas in the 45 patients with simplified acute physiologic scores lower than 16, noninvasive

**TABLE 2.** SERIOUS COMPLICATIONS AND COMPLICATIONS RESULTING IN DEATH.

VARIABLE*	NONINVASIVE-VENTILATION GROUP (N=32)	CONVENTIONAL-VENTILATION GROUP (N=32)
Patients with complications — no. (%)†	12 (38)	21 (66)
Patients with complications causing death in ICU — no.	9	15
No. of complications per patient‡	1.3	1.7
Death after discharge from ICU — no.	1	1
Complications — total no./no. causing death in ICU (% of group)§		
Myocardial infarction or cardiogenic shock	2/2 (6)	4/4 (12)
Sepsis¶	6/5 (19)	11/6 (34)
Renal failure	3/0 (9)	5/0 (16)
Pancreatitis	1/0 (3)	1/1 (3)
Polyneuropathy of the critically ill	0/0	1/0 (3)
Pneumonia	1/0 (3)	8/2 (25)§
Sinusitis	0/0	2/0 (6)
Pulmonary embolism	0/0	1/1 (3)
Massive blood loss	0/0	1/1 (3)
Infection at study entry**	2/2 (6)	0/0

\*ICU denotes intensive care unit.

†P=0.02 for the comparison between the groups.

‡Only patients with complications were included in this calculation.

§Complications related to the presence of the endotracheal tube (nine cases of pneumonia [four caused by *Pseudomonas aeruginosa*, three by methicillin-resistant *Staphylococcus aureus*, and two by acinetobacter] and two cases of sinusitis [both caused by *S. aureus*]) were more frequent in patients randomly assigned to conventional ventilation (10 patients [31 percent]) than in those switched to conventional ventilation after the failure of noninvasive ventilation (1 patient [3 percent], P=0.003). Ventilator-associated pneumonia was diagnosed in nine patients after 6±4 days of conventional ventilation. No patient had clinical or radiographic manifestations of pneumonia during noninvasive ventilation. All complications listed occurred in the intensive care unit.

¶In the conventional-ventilation group, in addition to pneumonia (eight patients), other sources of sepsis included mediastinitis (one patient), urinary tract infection (one patient), and catheter-related infection (one patient). Among the patients in the noninvasive-ventilation group, sources of infection included pneumonia diagnosed six days after endotracheal intubation in one patient in whom noninvasive ventilation failed, urinary tract infection (one patient), catheter-related infection (one patient), empyema (one patient), necrotizing fasciitis (one patient), and infection of tracheostomy stoma (after procedure was performed on day nine of mechanical ventilation) in one patient initially assigned to receive noninvasive ventilation, who required intubation. The two cases of sinusitis in the conventional-ventilation group occurred in two patients with nasotracheal intubation and did not cause sepsis. Three additional patients in whom facial skin necrosis developed during noninvasive ventilation had spontaneous healing within seven days.

||P=0.003 for the comparison of the rates of pneumonia and sinusitis combined in the two groups.

\*\*The two infections at study entry were due to intraabdominal sepsis in patients who had undergone colorectal surgery.

ventilation was superior to conventional ventilation (data not shown).

## DISCUSSION

We found that, with similar ventilator settings, noninvasive ventilation was as effective as conventional ventilation in improving gas exchange in patients

with acute hypoxemic respiratory failure. Furthermore, the rate of serious complications, in particular those related to intubation (pneumonia and sinusitis), was significantly lower in patients receiving noninvasive ventilation. Successful noninvasive ventilation was associated with shorter stays in the intensive care unit. Ten patients in whom noninvasive ventilation failed (31 percent of the group) required intubation despite an improvement in gas exchange; this finding agrees with a prior report.<sup>9</sup>

Noninvasive ventilation can relieve hypoxemic respiratory failure in patients with pneumonia, cardiogenic pulmonary edema, or postoperative complications.<sup>1</sup> Twenty-nine studies enrolling 748 patients described the successful application of noninvasive ventilation in patients with hypoxemic respiratory failure of various causes.<sup>1</sup> In one study, gas exchange improved when patients with hypoxemia had their endotracheal tubes replaced by noninvasive face masks with similar settings.<sup>25</sup>

In our study, the noninvasive-ventilation and conventional-ventilation groups had received a similar number of invasive devices, not counting the endotracheal tubes in the patients in the conventional-ventilation group. Endotracheal intubation is the single most important predisposing factor for ventilator-associated pneumonia.<sup>26</sup> We identified pneumonia using bronchoscopic criteria in eight patients in the conventional-ventilation group (25 percent). The presence or absence of nosocomial pneumonia helps determine the outcome of respiratory failure.<sup>26</sup> Two patients in the conventional-ventilation group died of ventilator-associated pneumonia. The low rate of ventilator-associated pneumonia among patients in the noninvasive-ventilation group is in agreement with other findings.<sup>1,5</sup>

As in other studies,<sup>5,13</sup> the outcome in patients with higher simplified acute physiologic scores was poor, irrespective of their randomization group. Among survivors, those in the noninvasive-ventilation group had a shorter duration of mechanical ventilation and a shorter stay in the intensive care unit. Factors that may have been involved in shortening the duration of mechanical ventilation include the avoidance of sedation, elimination of the extra work of breathing imposed by the endotracheal tube, the lower rate of ventilator-associated pneumonia, and earlier removal from ventilation. There were more patients with respiratory acidosis in the conventional-ventilation group, and this may have affected the duration of mechanical ventilation and the outcome in this group. However, in an earlier randomized study of patients without chronic obstructive pulmonary disease, patients with a PaCO<sub>2</sub> greater than 45 mm Hg who were treated with noninvasive ventilation had shorter durations of stay in the intensive care unit and a lower mortality rate than those treated with conventional ventilation.<sup>13</sup>

**TABLE 3.** CHARACTERISTICS OF PATIENTS ACCORDING TO THE SUCCESS OR FAILURE OF NONINVASIVE VENTILATION AND SURVIVAL OR DEATH IN THE CONVENTIONAL-VENTILATION GROUP.\*

VARIABLE	NONINVASIVE-VENTILATION GROUP (N=32)			CONVENTIONAL-VENTILATION GROUP (N=32)		
	INTUBATION NOT REQUIRED (N=22)	INTUBATION REQUIRED (N=10)	P VALUE	SURVIVED (N=17)	DIED (N=15)	P VALUE
Age (yr)	47±21	62±7	0.006	51±20	65±14	0.03
SAPS†	12±4	16±3	0.009	10±4	14±4	0.02
Causes of acute respiratory failure						
Pneumonia (no.)	4	1		2	2	
Trauma (no.)	4	0		3	1	
Cardiogenic pulmonary edema (no.)	4	3		2	3	
Postoperative (no.)	10	6		10	9	
No. of invasive devices per patient	4±1	5±1	0.12	5±1	6±1	0.006
Initial improvement in PaO <sub>2</sub> :FiO <sub>2</sub> (no.)	16	4	0.12	8	7	0.98
Sustained improvement in PaO <sub>2</sub> :FiO <sub>2</sub> (no.)	17	2	0.003	16	8	0.01
Duration of mechanical ventilation (days)‡	2±1	15±7	<0.001	6±5	9±9	0.23
Length of stay in intensive care unit (days)§	6±6	16±7	0.002	18±21	12±12	0.28
Discharged from intensive care unit (no.)	22	1	<0.001	17	0	
Septic complications after study entry (no.)¶						
Sepsis	1	5	0.006	5	6	0.53
Severe sepsis	0	3		0	5	
Septic shock	0	1		0	1	

\*Plus–minus values are means ±SD.

†SAPS denotes simplified acute physiologic score.<sup>23</sup> The range of possible values is 0 to 56.

‡For patients who underwent intubation after the failure of noninvasive ventilation, the duration of mechanical ventilation was the total period of ventilation.

§Patients who died in the intensive care unit are included. All complications listed occurred while patients were in the intensive care unit.

¶Causes of septic shock included necrotizing fasciitis (in the patient in the noninvasive-ventilation group) and pneumonia (in the patient in the conventional-ventilation group). Among the patients assigned to noninvasive ventilation who required intubation, all five patients who had septic complications died. Among the patients assigned to conventional ventilation, all patients who had severe sepsis or septic shock died.

In conclusion, we found that noninvasive ventilation was as effective as conventional ventilation in improving gas exchange in patients with acute hypoxemic respiratory failure, and that when endotracheal intubation was avoided, the development of ventilator-associated pneumonia was unlikely.

### REFERENCES

1. Meduri GU. Noninvasive positive-pressure ventilation in patients with acute respiratory failure. *Clin Chest Med* 1996;17:513-53.
2. Bott J, Carroll MP, Conway JH, et al. Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet* 1993;341:1555-7.
3. Ahmed AH, Fenwick L, Angus RM, Peacock AJ. Nasal ventilation v doxapram in the treatment of type II respiratory failure complicating chronic airflow obstruction. *Thorax* 1992;1:858. abstract.
4. Daskalopoulou E, Tsara V, Fekete K, Koutsantas V, Christaki P. Treatment of acute respiratory failure in COPD patients with positive airway pressure via nasal mask (NPPV). *Chest* 1993;103:Suppl:271S. abstract.
5. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333:817-22.
6. Martin TJ, Sanders MH, Bierman MI, Hovis JD. Non-invasive application of bi-level positive airway pressure to prevent endotracheal intubation in acute respiratory failure. *Crit Care Med* 1994;23:Suppl:A129. abstract.
7. Kramer N, Meyer TJ, Meharg J, Cece RD, Hill NS. Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 1995;151:1799-806.
8. Keenan SP, Kernerman PD, Cook DJ, Martin CM, McCormack D, Sibbald WJ. The effect of noninvasive positive pressure ventilation on mortality in patients admitted with acute respiratory failure: a meta-analysis. *Crit Care Med* 1997;25:1685-92.

9. Meduri GU, Turner RE, Abou-Shala N, Wunderink RG, Tolley E. Non-invasive positive pressure ventilation via face mask: first-line intervention in patients with acute hypercapnic and hypoxemic respiratory failure. *Chest* 1996;109:179-93.
10. Rasanen J, Heikkila J, Downs J, Nikki P, Vaisanen I, Viitanen A. Continuous positive airway pressure by face mask in acute cardiogenic pulmonary edema. *Am J Cardiol* 1985;55:296-300.
11. Bersten AD, Holt AW, Vedig AE, Skowronski GA, Baggoley CJ. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991;325:1825-30.
12. Lin M, Yang YF, Chiang HT, Chang MS, Chiang BN, Cheitlin MD. Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary edema: short-term results and long-term follow-up. *Chest* 1995;107:1379-86.
13. Wysocki M, Tric L, Wolff MA, Millet H, Herman B. Noninvasive pressure support ventilation in patients with acute respiratory failure: a randomized comparison with conventional therapy. *Chest* 1995;107:761-8.
14. Goris RJA, te Boekhorst TPA, Nuytink JKS, Gimbrere JS. Multiple-organ failure: generalized autodestructive inflammation? *Arch Surg* 1985;120:1109-15.
15. Brochard L, Harf A, Lorino H, Lemaire F. Inspiratory pressure support prevents diaphragmatic fatigue during weaning from mechanical ventilation. *Am Rev Respir Dis* 1989;139:513-21.
16. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1994;150:896-903.
17. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med* 1992;20:864-74.
18. Meduri GU, Mauldin GL, Wunderink RG, et al. Causes of fever and pulmonary densities in patients with clinical manifestations of ventilator-associated pneumonia. *Chest* 1994;106:221-35.
19. Antonelli M, Moro ML, Capelli O, et al. Risk factors for early onset pneumonia in trauma patients. *Chest* 1994;105:224-8.
20. Meduri GU, Chastre J. The standardization of bronchoscopic techniques for ventilator-associated pneumonia. *Chest* 1992;102:Suppl 1:557S-564S.

- 21.** Antonelli M, Conti G, Riccioni L, Meduri GU. Noninvasive positive-pressure ventilation via face mask during bronchoscopy with BAL in high-risk hypoxemic patients. *Chest* 1996;110:724-8.
- 22.** Bernard GR, Artigas A, Brigham KL. The American-European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994;149:818-24.
- 23.** Le Gall JR, Loirat P, Alperovitch A, et al. A simplified acute physiology score for ICU patients. *Crit Care Med* 1984;12:975-7.
- 24.** Snedecor GW, Cochran WG. *Statistical methods*. 6th ed. Ames: Iowa State University Press, 1967.
- 25.** Gregoretti C, Burbi L, Berardino M, et al. Non invasive mask ventilation (NIMV) in trauma and major burn patients. *Am Rev Respir Dis* 1992; 145:Suppl:A75. abstract.
- 26.** Estes RJ, Meduri GU. The pathogenesis of ventilator-associated pneumonia. I. Mechanisms of bacterial transcolonization and airway inoculation. *Intensive Care Med* 1995;21:365-83.