Characteristics and Outcomes in Adult Patients Receiving Mechanical Ventilation
A 28-Day International Study

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Context The outcome of patients receiving mechanical ventilation for particular indications has been studied, but the outcome in a large number of unselected, heterogeneous patients has not been reported.

Objective To determine the survival of patients receiving mechanical ventilation and the relative importance of factors influencing survival.

Design, Setting, and Subjects Prospective cohort of consecutive adult patients admitted to 361 intensive care units who received mechanical ventilation for more than 12 hours between March 1, 1998, and March 31, 1998. Data were collected on each patient at initiation of mechanical ventilation and daily throughout the course of mechanical ventilation for up to 28 days.

Main Outcome Measure All-cause mortality during intensive care unit stay.

Results Of the 15757 patients admitted, a total of 5183 (33%) received mechanical ventilation for a mean (SD) duration of 5.9 (7.2) days. The mean (SD) length of stay in the intensive care unit was 11.2 (13.7) days. Overall mortality rate in the intensive care unit was 30.7% (1590 patients) for the entire population, 52% (120) in patients who received ventilation because of acute respiratory distress syndrome, and 22% (115) in patients who received ventilation for an exacerbation of chronic obstructive pulmonary disease. Survival of unselected patients receiving mechanical ventilation for more than 12 hours was 69%. The main conditions independently associated with increased mortality were (1) factors present at the start of mechanical ventilation (odds ratio [OR], 2.98; 95% confidence interval [CI], 2.44-3.63; P<.001 for coma), (2) factors related to patient management (OR, 3.67; 95% CI, 2.02-6.66; P<.001 for plateau airway pressure >35 cm H₂O), and (3) developments occurring over the course of mechanical ventilation (OR, 8.71; 95% CI, 5.44-13.94; P<.001 for ratio of PaO₂ to fraction of inspired oxygen <100).

Conclusion Survival among mechanically ventilated patients depends not only on the factors present at the start of mechanical ventilation, but also on the development of complications and patient management in the intensive care unit.

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VENTILATION.

veloping over the course of mechanical tatory settings, and organ failure de-
tients, such as baseline characteristics at
ease, and cancer.
creased mortality were age, multiorgan
independently associated with an in-
pital mortality rate of 31%. The multi-
orcent prospective study in 132 ICUs from Sweden, Denmark,
and Iceland determined that 1231 pa-
tients required mechanical ventilation
more than 24 hours within the first
week after ICU admission; the 90-day
ortality was 41%. Age, acute physiol-
ogy score of more than 15, a nonpul-
monary origin of respiratory failure,
more than 2 quadrants with infiltrates,
and immunosuppression were indepen-
dently associated with outcome. A ret-
rospective cohort of 61 113 patients in
04 US hospitals yielded a 31-day hos-
pital mortality rate of 31%. The multi-
ivariate analysis showed that factors
independently associated with an in-
creased mortality were age, multiorgan
system failure, human immunodeficien-
cy virus infection, chronic liver dis-
ease, and cancer.

The objective of this study was to de-
termine the survival and the relative
importance of many factors influencing
survival of mechanically ventilated pa-
tients, such as baseline characteristics
the start of mechanical ventilation, ven-
tilatory settings, and organ failure de-
veloping over the course of mechanical
vention.

METHODS

Study Design

We conducted a prospective cohort
study of consecutive adult patients ad-
itted to 361 ICUs in 20 countries and
who received mechanical ventilation for
more than 12 consecutive hours be-
tween March 1, 1998, and March 31,
1998. Before data collection, the study
protocol was reviewed and approved by
institutional review committees of each
hospital.

To minimize behavior change as a re-
result of being observed, only the inves-
tigator and research coordinator in each
ICU were aware that the study was un-
der way. Each investigator and re-
search coordinator was provided with
a manual describing data collection and
definitions. Each country had a na-
tional coordinator who was able to an-
swer questions regarding data collect-
ion. Before the initiation of the study,
forms were completed for 10 patients in
3 different ICUs to evaluate their com-
prehensibility and reproducibility. Based
on difficulties detected during this ini-
tial evaluation, forms were modified be-
fore commencing the study. Each ques-
tionnaire was checked by 3 study
coordinators to identify omissions and
inconsistent data were corrected.

The following information was col-
ced in each patient: age, sex, weight,
simplified acute physiology score II
(SAPS II) at the time of admission to the
ICU, chronic functional status, indica-
tion for the initiation of mechanical ven-
tilation, and modality of ventilatory sup-
port (noninvasive or conventional
mechanical ventilation). The fol-
lowing events were assessed daily during
the course of mechanical ventilation for
a maximum of 28 days: need for tracheal
intubation in patients receiving nonin-
vasive mechanical ventilation, ARDS,
barotrauma, pneumonia, sepsis, renal
failure, hepatic failure, and coagulopa-
thy. Because sepsis, pneumonia, and
ARDS could be reasons for the initia-
tion of mechanical ventilation, they were
considered as events only if they ap-
peared more than 48 hours after me-
chanical ventilation was started. Acute
respiratory distress syndrome was de-
fined according to the criteria of the
American-European consensus confer-
ence. Sepsis and shock were defined
according to the criteria of the Ameri-
can College of Chest Physicians-
Society of Critical Care Medicine con-
sensus conference. Barotrauma refers
to the development of at least 1 of the
following: interstitial emphysema, pneu-
mothorax, pneumomediastinum, pneu-
monoperitonium, or subcutaneous
emphysema. Ventilator-associated pne-
monia was defined according to the
modified Centers for Disease Control
and Prevention criteria, which re-
quire a new radiographic infiltrate per-
sistent for 48 hours or more plus a body
temperature more than 38.5°C or less
than 35.0°C, a leukocyte count more than
10000/µL or less than 3000/µL, pu-
rulent sputum or change in character of
sputum, or isolation of pathogenic bac-
teria from an endotracheal aspirate. Re-
nal failure was defined as an acute in-
crease in creatinine of more than 2
mg/dL (177 µmol/L), double the base-
line value in a patient with underlying
chronic renal failure, and/or the need
for acute hemodialysis or acute use of
any form of dialysis. Hepatic failure was
defined as an acute change in bilirubin
to more than 2 mg/dL (34 µmol/L) with
transaminase and lactate dehydroge-
nase levels at least twice the upper
limit of normal. Coagulopathy was defined
as a decrease in the platelet count of 2%
or more from the baseline with an in-
crease in prothrombin time at least twice
the control value.

The first arterial blood gas measure-
ment and corresponding ventilator set-
tings were recorded daily while pa-
tients received mechanical ventilation for
a maximum of 28 days. The use of neu-
romuscular blockers, sedatives, and va-
soactive drugs (given for ≥ 3 hours dur-
ing a 24-hour period) was recorded daily
for a maximum of 28 days.

Duration of mechanical ventilation
was defined as the time elapsed from
the initiation of ventilatory support to
the onset of weaning. The onset of
weaning was the time that the physi-
cian in charge considered the patient
likely to resume and sustain spontane-
ous breathing. Weaning was per-
formed by either a reduction in the
level of ventilator support or a trial of spon-
taneous breathing. The need for rein-
tubation within 48 hours after extuba-
tion and the time of reintubation were recorded. All patients were followed up until hospital discharge.

**Statistical Analysis**

The primary outcome measure was all-cause mortality during ICU stay. All variables were grouped in 3 categories: factors present at the start of mechanical ventilation, factors related to patient management, and events occurring over the course of mechanical ventilation. The categorical variables, such as presence of particular manifestations, were coded as 0 (absence) or as 1 (presence). With respect to those variables grouped in the categories of factors related to patient management and events occurring over the course of mechanical ventilation, a patient was considered to have any of the above conditions if present for at least 2 consecutive days. For the PaO$_2$/FiO$_2$ ratio, the lowest value was selected. Some continuous variables (such as age, SAPS II score), positive end-expiratory pressure, tidal volume) were coded as dummy variables that compare all categories with that category having the lower mortality. The remaining continuous variables were dichotomized using cutoff points that were clinically relevant with previously published threshold values. For the univariate analysis, frequencies were compared by the χ$^2$ test and adjusted odds ratios, and 95% confidence intervals (CIs) were calculated. Comparison among groups according to the reason for initiating mechanical ventilation and events occurring over the course of mechanical ventilation were made using 1-way analysis of variance for continuous variables. The Kaplan–Meier method was used to determine the probability of survival over duration of ventilation.

To estimate the simultaneous effects of multiple variables on ICU mortality, a multivariate analysis was performed using a conditional logistic regression model and a forward stepwise selection method to correct for colinearity. The criterion for entering variables tested in the model were selected if P<.10. We used a logistic regression analysis in place of a Cox proportional hazards model because a large number of the variables did not satisfy the assumption of proportional hazards. Statistical analysis was performed with SPSS version 8.0 (SPSS Inc, Chicago, Ill).

**RESULTS**

Seventy-seven percent of the 361 ICUs included in the study were medical/surgical, 19% were medical, and 4% were surgical. Ninety percent of the participant ICUs were located at postgraduate teaching hospitals and 69% at pregraduate teaching hospitals. In the 361 ICUs, 15,757 patients were admitted during the study period and 5,183 (33%) received mechanical ventilation for more than 12 hours. A total of 5,131 (99%) patients were followed up during their entire course of mechanical ventilation and 52 (1%) were followed up for the first 28 days of ventilation. Demographic characteristics and the reasons for instituting mechanical ventilation are listed in **Table 1**.

Mechanical ventilation was delivered through an orotracheal tube in 4,614 (89.0%) patients, a nasotracheal tube in 211 (4.1%) patients, a facial mask in 256 (4.9%) patients (16.9% among patients ventilated because of an exacerbation of COPD), and a tracheostomy in 102 (2.0%) patients. Of the 256 patients who initially received noninvasive ventilation, 81 (31.6%) needed tracheal intubation. Eighty-five patients with COPD received noninvasive ventilation and 22 (25.9%) subsequently required tracheal intubation. Of the 148 patients with ARF who received noninvasive ventilation, 54 (36.5%) subsequently required tracheal intubation.

**Table 2** lists the duration of mechanical ventilation until weaning, the duration of weaning, length of ICU stay, and length of hospital stay according to the reason for initiating mechanical ventilation; the times for mechanical ventilation and weaning are exclusive of each other. The ventilator modes and settings at the time of obtaining blood samples were recorded. All patients were followed up until hospital discharge.

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Table 1. Characteristics of the Studied Patients on Admission to the Intensive Care Unit (ICU)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients Mechanically Ventilated (N = 5,183)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD) [median (IQR)], y</td>
<td>59.2 (17.3) [63 (48-73)]</td>
</tr>
<tr>
<td>Sex, females</td>
<td>1985 (38.7)</td>
</tr>
<tr>
<td>SAPS II score, mean (SD) [median (IQR)]</td>
<td>44.1 (17.0) [43 (32-54)]</td>
</tr>
<tr>
<td>Prior functional status, limited activity</td>
<td>2016 (38.9)</td>
</tr>
<tr>
<td>Medical/surgical</td>
<td>3,428 (66.1)/1,755 (33.9)</td>
</tr>
<tr>
<td>Reason for the initiation of mechanical ventilation</td>
<td></td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>3,564 (68.8)</td>
</tr>
<tr>
<td>Coma</td>
<td>864 (16.7)</td>
</tr>
<tr>
<td>Acute respiratory failure on chronic pulmonary disease</td>
<td>522 (10.1)</td>
</tr>
<tr>
<td>COPD</td>
<td>79 (1.5)</td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory disease (non-COPD)</td>
<td>60 (1.2)</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>94 (1.8)</td>
</tr>
</tbody>
</table>

| Cause of acute respiratory failure†               |                                                        |
| Postoperative                                     | 1,080 (20.8)                                          |
| Pneumonia                                         | 721 (13.9)                                            |
| Congestive heart failure                          | 539 (10.4)                                            |
| Sepsis                                            | 458 (8.8)                                             |
| Trauma                                            | 407 (7.9)                                             |
| ARDS                                              | 231 (4.5)                                             |
| Aspiration                                        | 129 (2.5)                                             |
| Cardiac arrest                                     | 100 (1.9)                                             |
| Other                                             | 367 (7.1)                                             |

*IQR indicates interquartile range; SAPS II, simplified acute physiology score II; COPD, chronic obstructive pulmonary disease; and ARDS, acute respiratory distress syndrome.
†More than 1 cause of acute respiratory failure per patient was permitted.
gases in the morning are listed in Table 3 according to the reason for initiating mechanical ventilation. Figure 1 shows the ventilator modes in the whole group over time.

A total of 5199 weaning attempts were undertaken in 3640 (70.2%) patients using the following methods: once-daily weaning trial in 2833 (77.8%) attempts, multiple weaning trials in 510 (14.0%) attempts, gradual reduction of pressure support in 752 (20.7%) attempts, gradual reduction of pressure in 872 (23.4%) attempts, flow-by in 32 (1.0%) attempts, and re-intubation within 48 hours (5.7% in the first 12 hours, 18.7% between 12 and 24 hours, 24.7% between 24 and 48 hours). Unplanned extubation was reported in 179 (3.4%) patients; of these patients, reintubation was required in 74 (41.3%) with 79.7% occurring in the first 12 hours after extubation, 9.5% between 12 and 24 hours, and 6.7% between 24 and 48 hours (time of reintubation of 3 patients was unknown).

Patients experienced the following during mechanical ventilation: barotrauma, 154 (3.0%); ARDS, 218 (4.4%); pneumonia, 439 (9.8%); sepsis, 457 (9.7%); shock, 1145 (22.1%); acute re-

### Table 2. Duration of Ventilator Support Until the Start of Weaning, Duration of Weaning, and Length of Stay in the Intensive Care Unit (ICU) and Hospital in Studied Patients*

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>COPD</th>
<th>ARDS</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of mechanical ventilation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) [Median (IQR)]</td>
<td>5.9 (7.2) [3-7]</td>
<td>5.1 (5.3) [4-6]</td>
<td>8.8 (5.8) [6-11]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Duration of weaning</strong></td>
<td>4.2 (7.2) [2-4]</td>
<td>4.7 (7.8) [2-5]</td>
<td>5.0 (5.8) [3-6]</td>
<td>.55</td>
</tr>
<tr>
<td><strong>Length of stay in ICU</strong></td>
<td>11.2 (13.7) [7-14]</td>
<td>11.2 (10.6) [8-13]</td>
<td>14.3 (17.7) [9-20]</td>
<td>.01</td>
</tr>
<tr>
<td><strong>Length of stay in hospital</strong></td>
<td>22.5 (23.7) [16-29]</td>
<td>21.2 (17.7) [17-27]</td>
<td>24.5 (24.8) [19-31]</td>
<td>.07</td>
</tr>
</tbody>
</table>

* COPD indicates chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; and IQR, interquartile range. P values are for comparisons between COPD and ARDS patients.

### Table 3. Ventilator Modes and Monitored Variables on Days 1, 3, and 7 of Mechanical Ventilation in Patients With an Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) or Acute Respiratory Distress Syndrome (ARDS)*

**Ventilator modes, No. (%)**

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>ARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/C</td>
<td>344 (65.9)</td>
<td>180 (63.6)</td>
</tr>
<tr>
<td>SIMV/PS</td>
<td>50 (9.6)</td>
<td>32 (11.3)</td>
</tr>
<tr>
<td>PS</td>
<td>40 (7.6)</td>
<td>24 (8.5)</td>
</tr>
<tr>
<td>PCV</td>
<td>20 (3.9)</td>
<td>11 (3.9)</td>
</tr>
<tr>
<td>SIMV</td>
<td>24 (4.6)</td>
<td>10 (3.5)</td>
</tr>
<tr>
<td>Other</td>
<td>39 (8.5)</td>
<td>26 (9.2)</td>
</tr>
</tbody>
</table>

**Monitored variables, mean (SD) [median (IQR)]**

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>ARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pressure, cm H2O</td>
<td>22 (6)</td>
<td>22 (6)</td>
</tr>
<tr>
<td>Plateau pressure, cm H2O†</td>
<td>586 (133)</td>
<td>564 (128)</td>
</tr>
<tr>
<td>Tidal volume, mL</td>
<td>8.4 (2.3)</td>
<td>8.0 (2.3)</td>
</tr>
<tr>
<td>Tidal volume, mL/kg</td>
<td>8.3 (6.7-10.0)</td>
<td>7.8 (6.4-9.9)</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>17 (6)</td>
<td>17 (6)</td>
</tr>
<tr>
<td>FiO2</td>
<td>0.52 (0.48-0.60)</td>
<td>0.46 (0.43-0.50)</td>
</tr>
</tbody>
</table>

**Patients without PEEP, No. (%)**

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>ARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP, cm H2O</td>
<td>5 (2)</td>
<td>5 (2)</td>
</tr>
</tbody>
</table>

*A/C indicates assist/control ventilation; SIMV, synchronized intermittent mandatory ventilation; PS, pressure support; PCV, pressure-controlled ventilation; IQR, interquartile range; and PEEP, positive end-expiratory pressure.
†Plateau pressure only recorded in patients ventilated with A/C.
nal failure, 971 (18.7%); hepatic failure, 326 (6.3%); coagulopathy, 552 (10.6%); respiratory acidosis, 288 (5.6%); and metabolic acidosis, 311 (6.0%).

Among the 5183 studied patients, 1590 died in the ICU (overall unit mortality: 30.7%). Of 4718 patients with known vital status at hospital discharge, 1876 were alive (hospital mortality: 39.2%).

**Figure 2** shows the Kaplan-Meier curves of the probability of survival over time of patients mechanically ventilated because of COPD, asthma, ARDS, and non-ARDS causes of ARF.

The ICU mortality associated with reintubation was 32.4% in patients with unplanned extubation and 22.6% in patients with planned extubation. The ICU mortality was 14.3% in patients with successful noninvasive ventilation and 42.0% in patients needing tracheal intubation after a failed attempt at noninvasive ventilation. Among patients with COPD ventilated because of ARF, ICU mortality was similar in those intubated after a failed attempt at noninvasive ventilation and in those treated with invasive ventilation (27.3% vs 23.8%, \( P = .91 \)). Conversely, among patients ventilated for ARF secondary to conditions other than COPD, those patients failing an attempt at noninvasive ventilation had a higher ICU mortality than those treated with invasive ventilation (48.1% vs 31.0%, \( P = .01 \)).

**Table 4** lists both the univariate and multivariate analysis of factors associated with ICU mortality. The following were factors independently associated with an increased mortality: age, SAPS II score at ICU admission, prior functional status characterized by limited activity, initiation of mechanical ventilation because of coma, ARDS, or sepsis, use of vasoactive drugs, use of neuromuscular blockers, peak pressure higher than 50 cm H₂O, plateau pressure higher than 35 cm H₂O, barotrauma, ARDS or sepsis developed after initiation of mechanical ventilation, \( \text{PaO}_2/\text{FiO}_2 \) ratio less than 200, and development of any of the following organ failures: cardiovascular (shock),...
### Table 4. Univariate and Multivariate Analysis of Factors Associated With Intensive Care Unit (ICU) Mortality in Ventilated Patients

<table>
<thead>
<tr>
<th>Factors Present at the Initiation of Mechanical Ventilation</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICU Mortality, %</strong> (95% Confidence Interval)</td>
<td><strong>Odds Ratio</strong> (95% Confidence Interval)</td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td><strong>Geographical area</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States and Canada</td>
<td>27 (25-29)</td>
<td>1.00</td>
</tr>
<tr>
<td>Europe</td>
<td>31 (29-33)</td>
<td>1.21 (1.04-1.40)</td>
</tr>
<tr>
<td>Latin America</td>
<td>34 (31-37)</td>
<td>1.38 (1.17-1.63)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>21 (19-24)</td>
<td>1.00</td>
</tr>
<tr>
<td>40-70</td>
<td>30 (28-32)</td>
<td>1.60 (1.33-1.91)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>36 (34-39)</td>
<td>2.11 (1.75-2.55)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (29-32)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (29-33)</td>
<td></td>
</tr>
<tr>
<td><strong>SAPS II score at ICU admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>15 (11-19)</td>
<td>1.00</td>
</tr>
<tr>
<td>20-39</td>
<td>19 (17-21)</td>
<td>1.31 (1.05-1.62)</td>
</tr>
<tr>
<td>40-59</td>
<td>35 (33-37)</td>
<td>3.06 (2.23-4.20)</td>
</tr>
<tr>
<td>60-80</td>
<td>50 (46-54)</td>
<td>5.72 (4.07-8.03)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>72 (64-79)</td>
<td>14.53 (9.01-23.22)</td>
</tr>
<tr>
<td><strong>Medical problem</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33 (31-35)</td>
<td>1.27 (1.16-1.39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Surgical problem</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-39</td>
<td>19 (17-21)</td>
<td>1.31 (1.19-1.45)</td>
</tr>
<tr>
<td>40-59</td>
<td>35 (33-37)</td>
<td>3.06 (2.23-4.20)</td>
</tr>
<tr>
<td>60-80</td>
<td>50 (46-54)</td>
<td>5.72 (4.07-8.03)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>72 (64-79)</td>
<td>14.53 (9.01-23.22)</td>
</tr>
<tr>
<td><strong>Prior functional status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>30 (28-32)</td>
<td>1.00</td>
</tr>
<tr>
<td>Limited activity</td>
<td>32 (30-34)</td>
<td>1.09 (1.00-1.19)</td>
</tr>
<tr>
<td><strong>Reason for initiation of mechanical ventilation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>31 (29-32)</td>
<td></td>
</tr>
<tr>
<td>Coma</td>
<td>36 (33-39)</td>
<td>1.31 (1.19-1.45)</td>
</tr>
<tr>
<td>COPD</td>
<td>22 (19-26)</td>
<td>0.70 (0.59-0.83)</td>
</tr>
<tr>
<td>Asthma</td>
<td>11 (8-21)</td>
<td>0.37 (0.20-0.68)</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>15 (9-24)</td>
<td>0.48 (0.30-0.78)</td>
</tr>
<tr>
<td><strong>Cause of acute respiratory failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative</td>
<td>22 (20-25)</td>
<td>0.67 (0.59-0.76)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>38 (35-42)</td>
<td>1.29 (1.16-1.43)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>28 (24-32)</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>55 (51-60)</td>
<td>1.95 (1.77-2.14)</td>
</tr>
<tr>
<td>Trauma</td>
<td>20 (17-25)</td>
<td>0.64 (0.53-0.79)</td>
</tr>
<tr>
<td>ARDS</td>
<td>52 (46-59)</td>
<td>1.76 (1.55-2.01)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>27 (20-36)</td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>44 (34-54)</td>
<td>1.45 (1.15-1.81)</td>
</tr>
<tr>
<td>Other</td>
<td>28 (23-33)</td>
<td></td>
</tr>
<tr>
<td><strong>Tidal volume, mL/kg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>32 (28-41)</td>
<td>1.23 (0.91-1.63)</td>
</tr>
<tr>
<td>6-10</td>
<td>30 (28-31)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;10</td>
<td>33 (30-35)</td>
<td>1.14 (0.99-1.31)</td>
</tr>
<tr>
<td><strong>PEEP, cm H₂O</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>28 (26-30)</td>
<td>1.00</td>
</tr>
<tr>
<td>5-10</td>
<td>31 (29-33)</td>
<td>1.15 (1.02-1.30)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>50 (44-56)</td>
<td>2.52 (1.96-3.24)</td>
</tr>
<tr>
<td><strong>Peak pressure &gt;50 cm H₂O</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 (53-74)</td>
<td>2.15 (1.83-2.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Plateau pressure &gt;35 cm H₂O</td>
<td>78 (69-86)</td>
<td>2.64 (2.36-2.95)</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>20 (17-23)</td>
<td>0.62 (0.52-0.74)</td>
</tr>
</tbody>
</table>

(continued)
renal failure, hepatic failure, coagulopathy, and metabolic acidosis.

**COMMENT**

Survival in patients with respiratory failure who required mechanical ventilation for more than 12 hours was 69% and depended not only on factors present when initiating mechanical ventilation but mainly on the development of complications, changes in monitored variables, and patient management during the subsequent course. Several studies have addressed the outcome of patients receiving mechanical ventilation but most of them have analyzed patients with a particular medical condition, such as ARDS or acute exacerbation of COPD. Three multicenter cohort studies evaluating patients requiring mechanical ventilation because of ARF of different etiologies have reported hospital mortality rates from 30% to 40%.

We recently published a study involving a large and unselected sample of mechanically ventilated patients, which yielded valuable information concerning epidemiology of mechanical ventilation, ventilatory modes, and ventilatory settings, however mortality and morbidity were not described. Strengths of the current study are that unselected mechanically ventilated patients were enrolled from different countries and 99% of the patients were screened daily over the duration of mechanical ventilation to evaluate the determinants of their outcome. Our study represents the largest study to our knowledge of a heterogeneous group of mechanically ventilated patients, which prospectively evaluates the effect of more than 30 variables potentially related to mortality after controlling for the effect of confounding factors.

A total of 25 published studies have reported the effect of age on the mortality of mechanically ventilated patients, but only 8 were prospective, 12 were based on populations with more than 100 elderly patients, and 9 had multivariate analysis. There are 6 prospective cohort studies evaluating whether age has an independent effect on the outcome of patients treated with mechanical ventilation after ICU admission and 5 found that age was independently associated with hospital mortality. Ely et al studied 300 mechanically ventilated patients admitted to medical and coronary ICUs and found that hospital mortality was 38.1% among patients older than 75 years and 38.8% among younger patients. The Cox proportional hazards analysis confirmed that survival did not differ between the 2 groups (relative risk for older patients, 0.82; 95% CI, 0.52-1.29). The study population, however, was small (67 patients >75 years) and represented a selected group enrolled in a clinical trial. The present study prospectively analyzes a number of unselected patients older than 70 years (n=1753) using a multivariate analysis to determine the effect of age on outcome. In the absence of a clearly defined threshold for elderly patients, the age cutoff has been arbitrarily chosen and has varied from more than 60 years to more than 85 years. Our data illustrate, after adjustment for other factors related to the mortality of mechanically ventilated patients, 3 intervals of age (<40, 40-70, >70 years) have very different prognostic value.

As reported in other studies, we found that men account for more than half of patients (61% males) receiving mechanical ventilation in the ICU. In a study combining surgical and medical
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patients, Kollef et al. using multivariate analysis showed that the hospital mortality rate was greater for female patients compared with male patients despite similar severity of illness and numbers of organ system derangements at the start of mechanical ventilation. In 580 medical patients, Epstein and Vuong showed that sex was not independently associated with hospital mortality after controlling for factors present at the start of mechanical ventilation and for development of acute hepatic failure and acute renal failure over the course of ventilation. The study by Luhr et al. in 1231 patients with ARF and RDS, also demonstrated that sex was not independently associated with mortality. We have taken into account many baseline and time dependent factors associated with mortality in a multivariate analysis, and our results show that mortality is not independently associated with the patient’s sex.

Clinicians may struggle with the decision to initiate invasive mechanical ventilation in patients with COPD because of concern about uncertain prognosis and prolonged mechanical ventilation. Our study found a hospital mortality of 28% in patients with COPD receiving mechanical ventilation due to an acute exacerbation of their disease. Two retrospective studies involving more than 150 patients with COPD requiring mechanical ventilation reported similar rates of hospital mortality of 32% and 28%. The major risk factors for hospital mortality are the development and severity of nonrespiratory organ system dysfunction and acute illness, while severity of the underlying respiratory function substantially influences mortality following hospital discharge. The univariate analysis in the present study showed that patients receiving mechanical ventilation due to an acute decompensation of COPD had significantly lower mortality than patients receiving mechanical ventilation because of ARF of other etiologies. However, when mortality was adjusted for the effect of organ system failures and variables related to both the acute severity of illness and patient management, the mortality rate of patients with COPD was not different from that of patients mechanically ventilated due to other etiologies of ARF. Mechanically ventilated patients with COPD had not only better clinical course than other mechanically ventilated patients but also duration of ventilatory support, duration of weaning, and length of ICU stay were not higher in mechanically ventilated patients with COPD when compared with patients ventilated due to other reasons of ARF. Ely et al. have also reported that duration of mechanical ventilation of patients with COPD was similar to that of other ventilated patients (5.5 vs 5 days).

Randomized trials evaluating the influence of different ventilator strategies on the outcome of patients with ARDS and/or acute lung injury have revealed contrary findings. Survival of control patients has ranged from 30% to 62%, whereas survival of patients in descriptive studies is about 40%, which is similar to the present finding. Investigators have shown that nonpulmonary organ failure markedly decreases survival in ARDS. Enrollment criteria that exclude patients with organ failure may partly explain the higher survival in clinical trials than in observational studies. Mortality may also differ depending on the type of organ failure. In the present study, cardiovascular failure (shock) and metabolic acidosis carried worse prognosis than coagulopathy. Most studies have used an organ system dysfunction index that scored each organ failure similarly; differences in survival rates among randomized trials and observational studies may be explained by imbalances resulting from the particular organ failure.

Another factor that may contribute to differences in reported outcomes is the point in the hospital course at which a patient develops ARDS. Croce et al. reported 2 distinct clinical entities of ARDS in trauma patients. One occurs within 48 hours of hospital admission and is associated with profound hemorrhagic shock, and the other occurs later and is associated with multiple system injury and pneumonia. Despite these differences, the overall mortality between patients with early ARDS and patients with late ARDS was similar. In the present study, survival was 23% lower in patients who developed ARDS 48 hours after the start of mechanical ventilation than in patients who had it when ventilation was instituted. Accordingly, it may be important to take into account the onset of ARDS when allocating patients in a clinical trial.

The reason for the initiation of mechanical ventilation influences the outcome of ventilated patients. After adjusting for other variables, the only factors independently associated with decreased survival were coma, ARDS, and sepsis, and the only factor independently associated with increased survival was postoperative state. The above findings are consistent with the results of other studies. Epstein and Vuong reported that both acute lung injury and sepsis leading to the initiation of mechanical ventilation were independently associated with an increased hospital mortality rate. Kollef et al. found that the presence of ARDS was independently associated with hospital mortality and that postoperative as an indication for mechanical ventilation was associated with a decreased mortality in the univariate analysis but not in the multivariate analysis. We have no information concerning whether patients included in the category of postoperative had urgent or elective surgery, but the finding that mortality is significantly decreased in postoperative patients seems to indicate that most patients had elective surgery.

Data from randomized trials of low tidal volumes in patients with ARDS have shown that increased survival with lower tidal volumes can be detected only when patients receiving traditional tidal volumes had mean plateau pressures more than 32 cm H₂O. Vasiyev et al. reported that a peak inspiratory pressure more than 50 cm H₂O at entry into the survey was associated with a survival rate of less than 20% while peak inspiratory pressure less than 30 cm H₂O was associated with a survival rate of...
60%. A retrospective description of all patients with ARDS treated in a Finnish hospital from 1993 through 1995 reported that both mean static end-inspiratory pressure and mortality decreased over the study period from 33 cm H₂O and 50%, respectively, in 1993 to 28 cm H₂O and 42% in 1994, and to 26 cm H₂O and 32% in 1995.22 Our study revealed an independent association between plateau pressure of more than 35 cm H₂O and decreased survival but did not prove that plateau pressure is causally related with the outcome of patients receiving mechanical ventilation. While development of nonpulmonary organ failures increased the risk of mortality in our study, development of pulmonary failure that resulted in a ratio of PaO₂/FIO₂ less than 100 carried an increased risk of mortality in our study, development of pulmonary organ failures increased the risk of mortality in patients with ARF, however, in the group of patients with ARDS, an independent association could be shown between a PaO₂/FIO₂ ratio less than 100 and mortality. Our study evaluates the effect of the pulmonary failure severity on the outcome of patients receiving mechanical ventilation with ARDS after controlling for the effect of a large number of other factors strongly associated with mortality, and also stratifies the severity of pulmonary failure according to mortality risk. In summary, both factors at baseline and complications of critical illness over time influence the outcome of patients receiving mechanical ventilation. Future controlled trials of ventilator strategies evaluating mortality need to take into account not only variables evident at the time of randomization but also developments that occur later in the course of mechanical ventilation.

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REFERENCES


