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

Andrés Esteban, MD, PhD
Antonio Anzueto, MD
Fernando Frutos, MD
Inmaculada Alía, MD
Laurent Brochard, MD
Thomas E. Stewart, MD
Salvador Benito, MD
Scott K. Epstein, MD
Carlos Apezteguía, MD
Peter Nightingale, MD
Alejandro C. Arroliga, MD
Martin J. Tobin, MD

Author Affiliations: Hospital Universitario de Getafe, Madrid, Spain (Dr Esteban, Frutos, and Alía); University of Texas Health Science Center, San Antonio (Dr Anzueto); Hôpital Henri Mondor, Créteil, France (Dr Brochard); Mount Sinai Hospital, University of Toronto, Toronto, Ontario (Dr Stewart); Hospital Sant Pau, Barcelona, Spain (Dr Benito); Tupper Research Institute, New England Medical Center, Boston, Mass (Dr Epstein); Hospital Professor Posadas, Buenos Aires, Argentina (Dr Apezteguía); South Manchester University Hospital, Manchester, England (Dr Nightingale); The Cleveland Clinic Foundation, Cleveland, Ohio (Dr Arroliga); and Loyola University of Chicago and Hines Veterans Affairs Hospital, Maywood, Ill (Dr Tobin).

Members of the Mechanical Ventilation International Study Group are listed at the end of this article.

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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reflecting restrictive, inclusion criteria en-
rolling less severely-ill patients. For ex-
ample, 88% of patients screened for the
ARDS Network trial were excluded; m-
mortality in these patients was higher
than those included in the trial.11

Vasilev et al12 conducted an inter-
national multicenter prospective study
to determine the hospital survival rates
of patients with acute respiratory fail-
ure (ARF) managed in the intensive care
unit (ICU). Of 1426 patients admitted
to ICUs from 11 centers in the United
States and 14 centers in Europe, 633 pa-
tients (44%) died in the hospital. Uni-
ivariate analysis revealed that the most
important predictors of hospital sur-
vival were severity of lung dysfunction,
etiology of ARF, and multiorgan dysfunc-
tion. Another prospective study13 in
132 ICUs from Sweden, Denmark,
and Iceland determined that 1231 pa-
tients required mechanical ventilation
for more than 24 hours within the first
week after ICU admission; the 90-day
mortality was 41%. Age, acute physi-
ology 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 re-
rospective cohort14 of 61 113 patients in
904 US hospitals yielded a 31-day hos-
ital mortality rate of 31%. The multi-
ivariate analysis showed that factors
independently associated with an in-
creased mortality were age, multiorgan
system failure, human immunodefi-
ciency virus infection, chronic liver dis-
ease, and cancer.

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

METHODS

Study Design

We conducted a prospective cohort
study of consecutive adult patients ad-
mitted 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-
tion. 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-
lected 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).15 The follow-
ing 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-
defined according to the criteria of the
American-European consensus confer-
ence.16 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.17 Barotrauma refers
to the development of at least 1 of the
following: interstitial emphysema, pneu-
mothorax, pneumomediastinum,
pneumoperitoneum, or subcutaneous
emphysema. Ventilator-associated pneu-
monia was defined according to the
modified Centers for Disease Control
and Prevention criteria,18 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 of 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.
Renal 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 de-
efined as an acute change in bilirubin to
more than 2 mg/dL (34 µmol/L) with
transaminase and lactic dehydroge-
nase levels at least twice the upper limit
of normal. Coagulopathy was defined as
a decrease in the platelet count of 25% 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.19-21 The onset of
weaning was the time that the physi-
ician charged considered the patient
likely to resume and sustain sponta-
nous 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 extub-
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 PaO2/FIO2 ratio, the lowest value was selected. Some continuous variables (such as age, SAPS II score, PaO2/FIO2 ratio, 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 χ² test and adjusted odds ratios, and 95% confidence intervals (CIs) were calculated. Comparison among groups according to the reason for initiating mechanical ventilation and weaning were exclusive 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 participants were located at postgraduate teaching hospitals and 69% at pregraduate teaching hospitals. In the 361 ICUs, 15757 patients were admitted during the study period and 3183 (33%) received mechanical ventilation for more than 12 hours. A total of 5131 (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 4614 (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

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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 = 5183)</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>3428 (66.1)/1755 (33.9)</td>
</tr>
<tr>
<td>Reason for the initiation of mechanical ventilation</td>
<td></td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>3564 (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></td>
</tr>
<tr>
<td>COPD</td>
<td>522 (10.1)</td>
</tr>
<tr>
<td>Asthma</td>
<td>79 (1.5)</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>
<tr>
<td>Cause of acute respiratory failure†</td>
<td></td>
</tr>
<tr>
<td>Postoperative</td>
<td>1080 (20.8)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>721 (13.9)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>539 (10.4)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>458 (8.8)</td>
</tr>
<tr>
<td>Trauma</td>
<td>407 (7.9)</td>
</tr>
<tr>
<td>ARDS</td>
<td>231 (4.5)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>129 (2.5)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>100 (1.9)</td>
</tr>
<tr>
<td>Other</td>
<td>367 (7.1)</td>
</tr>
</tbody>
</table>

*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.

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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, gradual reduction of pressure support in 510 (14.0%) attempts, gradual reduction of synchronized intermittent mandatory ventilation in 311 (8.5%) attempts, and flow-by in 32 (1.0%) attempts.

Deliberate extubation was performed in 2858 (55.1%) patients; of these patients, 350 (12.2%) required reintubation within 48 hours (56.5% 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>Duration, Mean (SD) [Median [IQR]], d</th>
<th>Overall</th>
<th>COPD</th>
<th>ARDS</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of mechanical ventilation</td>
<td>5.9 (7.2) [3 {2-7}]</td>
<td>5.1 (5.3) [4 {2-6}]</td>
<td>8.8 (8.5) [6 {3-11}]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration of weaning</td>
<td>4.2 (7.2) [2 {1-4}]</td>
<td>4.7 (7.8) [2 {1-5}]</td>
<td>5.0 (5.6) [3 {1-6}]</td>
<td>.55</td>
</tr>
<tr>
<td>Length of stay in ICU</td>
<td>11.2 (13.7) [7 {4-14}]</td>
<td>11.2 (10.6) [8 {5-13}]</td>
<td>14.3 (17.7) [9 {5-20}]</td>
<td>.07</td>
</tr>
<tr>
<td>Length of stay in hospital</td>
<td>22.5 (23.7) [16 {9-29}]</td>
<td>21.2 (17.7) [17 {10-27}]</td>
<td>24.5 (24.8) [19 {9-31}]</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)

<table>
<thead>
<tr>
<th>Ventilator modes, No. (%)</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>

<table>
<thead>
<tr>
<th>Monitored variables, mean (SD) [median [IQR]]</th>
<th>Overall</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>
<td>25 (6)</td>
</tr>
<tr>
<td>Tidal volume, mL</td>
<td>586 (133) [500-692]</td>
<td>564 (128) [500-640]</td>
<td>589 (135) [500-670]</td>
</tr>
<tr>
<td>Tidal volume, mL/kg</td>
<td>8.4 (2.3) [8.3-10.0]</td>
<td>8.0 (2.3) [7.6-9.6]</td>
<td>8.1 (2.6) [7.9-10.0]</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>17 (6) [16-14]</td>
<td>17 (6) [16-14]</td>
<td>17 (6) [18-12]</td>
</tr>
<tr>
<td>FiO2</td>
<td>52 (18) [50-60]</td>
<td>46 (13) [40-60]</td>
<td>50 (18) [40-60]</td>
</tr>
</tbody>
</table>

Patients without PEEP, No. (%) 218 (47.6) 128 (45.2) 33 (38.8) 34 (16.0) 14 (8.0) 8 (9.7)

PEEP, cm H2O 5 (2) 5 (2) 6 (3) 8 (4) 9 (3) 9 (3)

* 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, PaO2/FiO2 ratio less than 200, and development of any of the following organ failures: cardiovascular (shock),

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## 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>ICU Mortality, % (95% Confidence Interval)</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Odds Ratio</strong> (95% CI)</td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td>Geographical area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States and Canada</td>
<td>27 (25-29)</td>
<td>1.00</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Europe</td>
<td>31 (29-33)</td>
<td>1.21 (1.04-1.40)</td>
<td>.001</td>
</tr>
<tr>
<td>Latin America</td>
<td>34 (31-37)</td>
<td>1.38 (1.17-1.63)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>21 (19-24)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>40-70</td>
<td>30 (28-32)</td>
<td>1.60 (1.33-1.91)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;70</td>
<td>36 (34-39)</td>
<td>2.11 (1.75-2.55)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (29-32)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (29-33)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>SAPS II score at ICU admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>15 (11-19)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>20-39</td>
<td>19 (17-21)</td>
<td>1.31 (0.95-1.82)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>40-59</td>
<td>35 (33-37)</td>
<td>3.06 (2.23-4.20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>60-80</td>
<td>50 (46-54)</td>
<td>5.72 (4.07-8.03)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;80</td>
<td>72 (64-79)</td>
<td>14.53 (9.01-23.22)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medical problem</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>30 (28-32)</td>
<td>1.00</td>
<td>.04</td>
</tr>
<tr>
<td>Limited activity</td>
<td>32 (30-34)</td>
<td>1.09 (1.00-1.19)</td>
<td>1.18 (1.02-1.39)</td>
</tr>
<tr>
<td>Reason for initiation of mechanical ventilation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>31 (29-32)</td>
<td>1.31 (1.19-1.45)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Coma</td>
<td>36 (33-39)</td>
<td>1.31 (1.19-1.45)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>COPD</td>
<td>22 (19-26)</td>
<td>0.70 (0.59-0.83)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Asthma</td>
<td>11 (6-21)</td>
<td>0.37 (0.20-0.68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>15 (9-24)</td>
<td>0.48 (0.30-0.78)</td>
<td>.001</td>
</tr>
<tr>
<td>Cause of acute respiratory failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative</td>
<td>22 (20-25)</td>
<td>0.67 (0.59-0.76)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>38 (35-42)</td>
<td>1.29 (1.16-1.43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>28 (24-32)</td>
<td>1.95 (1.77-2.14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>55 (51-60)</td>
<td>1.95 (1.77-2.14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Trauma</td>
<td>20 (17-25)</td>
<td>0.64 (0.53-0.79)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ARDS</td>
<td>52 (46-59)</td>
<td>1.76 (1.55-2.01)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Aspiration</td>
<td>27 (20-36)</td>
<td>1.45 (1.15-1.81)</td>
<td>.004</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>44 (34-54)</td>
<td>1.45 (1.15-1.81)</td>
<td>.004</td>
</tr>
<tr>
<td>Other</td>
<td>28 (23-33)</td>
<td>1.45 (1.15-1.81)</td>
<td>.004</td>
</tr>
<tr>
<td>Factors Related to Patient Management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful noninvasive ventilation</td>
<td>14 (10-21)</td>
<td>0.46 (0.32-0.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of vasoactive drugs</td>
<td>48 (46-50)</td>
<td>2.41 (2.22-2.63)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of sedatives</td>
<td>33 (31-35)</td>
<td>1.22 (1.13-1.34)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Use of neuromuscular blockers</td>
<td>50 (46-55)</td>
<td>1.75 (1.58-1.94)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tidal volume, mL/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>32 (28-41)</td>
<td>1.23 (0.91-1.63)</td>
<td>.09</td>
</tr>
<tr>
<td>6-10</td>
<td>30 (28-31)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>33 (30-35)</td>
<td>1.14 (0.99-1.31)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PEEP, cm H₂O</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>28 (26-30)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td>31 (29-33)</td>
<td>1.15 (1.02-1.30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;10</td>
<td>50 (44-56)</td>
<td>2.52 (1.96-3.24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Peak pressure &gt;50 cm H₂O</td>
<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>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>20 (17-23)</td>
<td>0.62 (0.52-0.74)</td>
<td>&lt;.001</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
patients, Kollef et al26 using multivariate analysis showed that the hospital mortality rate was greater for female pa-
tients compared with male patients de-
spite similar severity of illness and num-
ber of organ system derangements at the
start of mechanical ventilation. In 580
medical patients, Epstein and Vuong29
showed that sex was not independently
associated with hospital mortality after
controlling for factors present at the start
of mechanical ventilation and for develop-
ment of acute hepatic failure and acute
renal failure over the course of ventila-
tion. The study by Luhr et al13 in 1231
patients with ARF and RDS, also dem-
strated that sex was not independ-
ently associated with mortality. We
have taken into account many baseline
and time dependent factors associated
with mortality in a multivariate analy-
sis, and our results show that mortality
is not independently associated with the
patient’s sex.

Clinicians may struggle with the de-
cision to initiate invasive mechanical
ventilation in patients with COPD be-
cause of concern about uncertain prog-
osis and prolonged mechanical ventila-
tion. Our study found a hospital mortal-
ity of 28% in patients with COPD receiv-
ing mechanical ventilation due to an
acute exacerbation of their disease.
Two retrospective studies involving
more than 150 patients with COPD re-
quiring mechanical ventilation reported
similar rates of hospital mortality of 32% and 28%.15,24 The major risk
factors for hospital mortality are the de-
velopment and severity of nonrespira-
tory organ system dysfunction and acute
illness, while severity of the underly-
ing respiratory function substantially
influences mortality following hospital dis-
charge.15,24 The univariate analysis in the
present study showed that patients re-
ceiving mechanical ventilation due to an
acute decompensation of COPD had signi-
ficantly lower mortality than pa-
tients receiving mechanical ventilation
because of ARF of other etiologies. How-
ever, when mortality was adjusted for
the effect of organ system failures and vari-
ables 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 me-
chanically ventilated due to other eti-
ologies of ARF. Mechanically venti-
lated patients with COPD had not only
better clinical course than other me-
chanically ventilated patients but also
duration of ventilatory support, dura-
tion of weaning, and length of ICU stay
were not higher in mechanically venti-
lated patients with COPD when com-
pared with patients ventilated due to
other reasons of ARF. Ely et al26 have also
reported that duration of mechanical
ventilation of patients with COPD was
similar to that of other ventilated pa-
tients (5.5 vs 5 days).

Randomized trials evaluating the in-
fluence of different ventilator stra-
egies on the outcome of patients with
ARDS and/or acute lung injury have
revealed contrary findings.2,25 Survival
of control patients has ranged from 30%
to 62%, whereas survival of patients in
descriptive studies is about 40%,7,10
which is similar to the present finding.
Investigators have shown that non-
pulmonary organ failure markedly
decreases survival in ARDS.7-10,22,23,31
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, car-
diovascular failure (shock) and meta-
bolic acidosis carried worse prognosis
than coagulopathy. Most studies have
used an organ system dysfunction index
that scored each organ failure simi-
larly; differences in survival rates among
randomized trials and observational
studies may be explained by imbal-
ances 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 al22 re-
port 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 differ-
ences, the overall mortality between pa-
tients with early ARDS and patients with
late ARDS was similar. In the present
study, survival was 23% lower in pa-
tients who developed ARDS 48 hours
after the start of mechanical ventilation
than in patients who had it when ven-
tilation was instituted. Accordingly, it
may be important to take into account
the onset of ARDS when allocating pa-
tients in a clinical trial.

The reason for the initiation of me-
chanical ventilation influences the out-
come of ventilated patients. After ad-
justing for other variables, the only
factors independently associated with
decreased survival were coma, ARDS,
and sepsis, and the only factor indepen-
dently associated with increased sur-
vival was postoperative state. The above
findings are consistent with the results
of other studies. Epstein and Vuong29 re-
ported that both acute lung injury and
sepsis leading to the initiation of me-
chanical ventilation were indepen-
dently associated with an increased hos-
pital mortality rate. Kollef et al26 found
that the presence of ARDS was indepen-
dently associated with hospital mortal-
ity and that postoperative as an indica-
tion for mechanical ventilation was
associated with a decreased mortality in
the univariate analysis but not in the
multivariate analysis. We have no infor-
mation concerning whether
patients included in the category of post-
operative had urgent or elective sur-
gery, but the finding that mortality is sig-
nificantly decreased in postoperative
patients seems to indicate that most pa-
tients 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.33 Vasiliev et al12
reported that a peak inspiratory pres-
sure more than 50 cm H2O at entry into
the survey was associated with a sur-
vival rate of less than 20% while peak
inspiratory pressure less than 30 cm H2O
was associated with a survival rate of
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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. 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 even higher risk. However, we have not stratified the degree of renal or hepatic functional impairment in patients developing either renal or hepatic dysfunction over the course of mechanical ventilation, so it is possible that severe renal or hepatic failure carries a similar risk of mortality than a ratio of PaO₂/FIO₂ less than 100.

The relationship between pulmonary failure and mortality has been extensively evaluated in studies involving patients receiving mechanical ventilation with ARDS, but results show considerable discrepancy. Doyle et al did not find any significant difference in hospital mortality between patients with a PaO₂/FIO₂ ratio of less than 150 at the time of entry into the study and those with a PaO₂/FIO₂ ratio between 150 and 299 (56% vs 59%). Krafft et al evaluated 101 published studies investigating 3264 patients with ARDS and found that no correlation existed between PaO₂/FIO₂ and mortality rates. On the contrary, Sloane et al and Knaus et al reported that mortality was higher in ARDS patients with an initial PaO₂/FIO₂ ratio less than 150. Navarrete-Navarro et al found that the PaO₂/FIO₂ ratio on the third day after the onset of ARDS was independently associated with increased mortality. Vasi-lyev et al reported that hospital survival rates increased as the PaO₂/FIO₂ ratio decreased, in such a way that hospital survival rate was 19% in patients with a PaO₂/FIO₂ ratio less than 100, 37.3% in patients with a PaO₂/FIO₂ ratio between 100 and 174, 50.0% in patients with a PaO₂/FIO₂ ratio between 175 and 224, and 70% in patients with a PaO₂/FIO₂ ratio higher than 225. Luhr et al reported that impaired oxygenation as manifested by a PaO₂/FIO₂ ratio of less than 200 was not significantly associated with 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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The Mechanical Ventilation International Study Group members include Argentina: F. Pálizas (Coordinator), R. Alasino (Hospital Municipal de Urgencias, Mendoza); R. Barzanelli (Hospital de la Firma Revol); J. Berón (Hospital Pablo Soria, San Salvador); C. Bevilacqua (Clinica Modelo de Morón, Morón); M. Cafaro (Hospital Regional Rio Gallegos, Rio Gallegos); E. Capparelli (Hospital Evita, Buenos Aires); G. Cardonatti (Hospital San Isidro, San Isidro); R. Correa (Hospital Central, Mendoza); A. Diez (Hospital Provincial de Centenario, Rosario); E. Estensoro (Hospital Escuela José de San Martín, La Plata); I. F. de Viana (Clinica San Martín, San Martín); A. Galevama (Hospital Zonal Bariloche, Bariloche); C. Galletti (Sanatorio Allende, Córdoba); G. García (Hospital Clemente Álvarez, Rosario); G. Gelardi (Hospital Privado del Sur, Bahía Blanca); S. Giannasi (Hospital Italiano, Buenos Aires); R. Guidi (Hospital Italiano Garibaldi, Rosario); L. Huespe Gardel (Hospital Escuela José F. de San Martín, Corrientes); C. Izraazl (Hospital de Clínicas de San Martín, Buenos Aires); O. López (Sanatorio Santa Isabel, Buenos Aires); G. Menga (Hospital María Ferrer, Buenos Aires); O. Otero (Centro Oncológico de Excelencia, Connet); F. Pálizas (Clinica Baztic-Perú, Buenos Aires); P. Pardo (Sanatorio de la Trinidad, Buenos Aires); C. Plaza (Sanatorio Julio Méndez, Buenos Aires); G. Raimondi (FLENI, Buenos Aires); A. Raimondi (Sanatorio Mater Dei, Buenos Aires); E. Romo (Hospital Privado Central); L. de Rosa (Sanatorio Quintar, San Salvador); C. Sáez (Sanatorio Británico, Rosario); A. Sansino (Hospital Juan A. Fernández, Buenos Aires); P. Schoon (Hospital Prof. Luis Gómez, Hiedra); C. Sola (Hospital José Penna, Bahía Blanca); C. Stölzting (Hospital Guillermo Rawson, San Juan); J. Taccone (Instituto Alfredo Lanari, Buenos Aires); C. Tolosa (Hospital Córdoba, Córdoba); M. Torreño (Sanatorio Modelo Quilmes, Quilmes); E. Turchetto (Hospital Privado de la Comunidad, Mar de Plata); R. Valente (CEMIC, Buenos Aires); R. Vargas (Políclinico Neuquén, Neuquén); L. Vasta (Sanatorio San Patricio, Buenos Aires); L. Vázquez (Hospital Español, Godoy Cruz); Vetere (Hospital Israelita Ezrach, Buenos Aires); F. Villarejo (Hospital Prof. Alejandro Posadas, Hiedra); N. Wainstein (Hospital Privado Fundación Favaron, Buenos Aires); O. Yunk (Hospital Español, Buenos Aires); G. Zabert (Clinica Pasteur, Neuquén).

BOLIVIA: F. Sandi Lora (Coordinator), L. Moya (Hospital Juan XXIII, La Paz); E. Salazar (Hospital Japonés, Santa Cruz); J. Zapata (Hospital Obrero, La Paz).

BRAZIL: C.M. David (Coordinator), SM Azevedo Lobo (Hospital de Base de São José do Rio Preto, São José do Rio Preto); A.B. de Almeida (Hospital de Clínicas da Universidade Federal, Uberlândia); MA Braga (Hospital Biocor, Belo Horizonte); I. Busetalo Chen (Hospital Nossa Senhora das Graças, Curitiba); M. Chaves Cavedio de Melo (Hospital São Lucas, Belo Horizonte); RN Daichik (Hospital Prontocor, Belo Horizonte); M. Contreras (Hospital Clementino Fraga Filho, Rio de Janeiro); R. Goldstein Alheira Rocha (Hospital Samaritano, São Paulo); R. de Macedo Bosco (Hospital Madre Teresa, Belo Horizonte); J.M. Nogueira (Hospital Universitario São José. Belo Horizonte); E. Oliveira (Hospital Vera Cruz, Belo Horizonte); S.F. Pinto (Casa de Saúde São José, Campo Grande); S.F. Pinto (Santa Casa de Campo Grande, Campo Grande); S.F. Pinto (Univ. Federal do Mato Grosso do Sul, Campo Grande); J.L. da Rocha Paranhos (Santa Casa de Misericórdia, São João do Sul); R. de Macedo Bosco (Hospital Samaritano, São Paulo); R. de Macedo Bosco (Hospital Madre Teresa, Belo Horizonte); J.M. Nogueira (Hospital Universitario São José. Belo Horizonte); E. Oliveira (Hospital Vera Cruz, Belo Horizonte); S.F. Pinto (Casa de Saúde São José, Campo Grande); S.F. Pinto (Santa Casa de Campo Grande, Campo Grande); S.F. Pinto (Univ. Federal do Mato Grosso do Sul, Campo Grande); L.R. de Siqueira Musolino (Irmandade da Santa Casa de Misericórdia, São Paulo).

CANADA: R. Fowler (Wellesley-Central Hospital, Toronto); J. Granton (Toronto Hospital General Division, Toronto); J. Granton (Toronto Hospital Western Division, Toronto); R. Hodder (Ottawa Civic Hospital, Ottawa); B. Kishin (Peel Memorial Hospital, Brampton-Ontario); S. Lapinsky (Mount Sinai Hospital, Toronto); D. Mazer (St. Michael’s Hospital, Toronto); D. Mean (Sunnymbrook Health Sciences Centre, Toronto); T. Rogovein (St. Joseph’s Health Centre, Toronto).

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L. Soto (Coordinator), G. Bugedo (Hospital Pontificia Universidad Católica de Valparaíso), C. Arroyo (Instituto Nacional del Tórax, Santiago), C. Ortega (Hospital Regional Concepción, Concepción), L. Soto (Hospital de Coquimbo, Coquimbo), S. León (Hospital de Arica y Parinacota), J. Cabezas (Hospital Universitario de Cuenca), L. De la Fuente (Hospital Universitario Reina Sofia, Cordoba), J. Llombart (Hospital Universitario de Alcalá del Henares), C. Acín (Hospital Universitario de La Princesa, Madrid).
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REFERENCES


