The Changing Face of Organ Failure in ARDS*

Mary R. Suchyta, DO, FCCP; James F. Orme, Jr, MD; and Alan H. Morris, MD

Objective: To study morbidity and mortality in ARDS patients from 1987 to 1999.

Design: Review of a prospectively collected database of ARDS patients.

Setting: Large, community hospital located in Salt Lake City, UT.

Patients: ARDS patients identified for the years 1987 to 1999. We prospectively identified ARDS patients at LDS Hospital in Salt Lake City, UT, using PaO2/fraction of inspired oxygen ratio (P/F) criteria, the presence of bilateral chest radiograph infiltrates, and the absence of left atrial hypertension.

Measurements: We assigned a primary risk factor for ARDS and identified the presence of organ failure before and after ARDS. We compared two temporal groups (ie, 1987 to 1990 vs 1994 to 1999) and used two criteria of arterial hypoxemia (P/F: patients from 1994 to 1999, ≤ 105 and ≤ 173; patients from 1987 to 1990, ≤ 0.2). At 1,500 m (the altitude of Salt Lake City), a PaO2 of ≤ 173 corresponds to an alveolar-arterial oxygen pressure difference of ≤ 200 at sea level. We used death at hospital discharge as an end point.

Main results: We identified 516 ARDS patients with a P/F of ≤ 105 (1987 to 1990, 256 patients; 1994 to 1999, 260 patients). Patients who had ARDS between 1994 and 1999 with a P/F of ≤ 105 had a lower mortality rate than patients between 1987 and 1990 with a P/F of ≤ 105 (44% vs 54%, respectively; p < .05). There were 288 patients with a P/F range of 106 to 173 during 1994 to 1999. Patients from 1994 to 1999 with a P/F of ≤ 173 had a lower mortality rate compared to patients from 1987 to 1990 (35% vs 54%, respectively; p < .01). Patients from 1994 to 1999 (for both P/F groups) had statistically fewer total nonpulmonary organ failures (ie, more patients had zero organ failures or single organ failures) and fewer specific organ failures (ie, sepsis, cardiovascular failures, and CNS failures). There were statistically fewer cases of cardiovascular failure, sepsis, and in both periods (ie, prior to ARDS and after the onset of ARDS) for 1994-to-1999 patients with a P/F of ≤ 105 compared to 1987-to-1990 patients with a P/F of ≤ 105.

Conclusions: Mortality from ARDS has decreased and is associated with decreased organ failure prior to and during the course of ARDS.

Key words: ARDS; arterial oxygenation; distributions; mortality; organ failure

Abbreviations: APACHE = acute physiology and chronic health evaluation; FIO2 = fraction of inspired oxygen; P(A-a)O2 = alveolar-arterial oxygen pressure difference; P/F = PaO2/fraction of inspired oxygen ratio; Pw = pulmonary capillary wedge pressure

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Reported mortality in ARDS patients varies from 30 to 50%.1-3 These values are lower than those previously reported.4-5 Zilberberg and Epstein2 reported that the lower mortality in ARDS was independent of the initial level of arterial oxygenation. The North American-European Consensus Conference redefined the criteria for ARDS.6 These new criteria require less severe arterial hypoxemia and may identify less severely injured patients than did previous criteria. This may explain some of the recently observed reductions in mortality from ARDS.
Longitudinal studies of ARDS at the same institution, using constant selection criteria are infrequent. During the 1980s, Milberg et al6 noted decreased mortality over an 11-year period using a constant definition of ARDS at a single institution. Abel et al7 also described a marked reduction in mortality for a small group of patients over a 7-year period during the 1990s in the United Kingdom. While these two studies reported decreased mortality, the paucity of longitudinal studies compromises conclusions about why ARDS mortality is changing.

There are other reasons for the uncertainty regarding ARDS mortality. Included among these are changes in risk factor distribution for the development of ARDS, changes in physician reporting of ARDS patients or secular changes in care. In addition, patient host factors may be different due to changes in health care (ie, new drugs). All of the above changes might influence the development of organ failure during ARDS, with an effect on mortality. Noting a gap in the literature, we tested the hypotheses that organ failure during ARDS has changed, and that this change is associated with decreased mortality.

**Materials and Methods**

We prospectively identified ARDS patients at the LDS Hospital in Salt Lake City, UT (Table 1). From May 1987 to December 1990, we identified ARDS patients by the presence of all of the following conditions: (1) acute onset of lung injury requiring endotracheal intubation and mechanical ventilation; (2) alveolar-arterial oxygen pressure difference (P\(\text{A0}_2\)/\(\text{O}_2\)) of \(\leq 0.2\); (3) pulmonary capillary wedge pressure (Pw) of \(\leq 15\) mm Hg or no evidence of left atrial hypertension; (4) total static thoracic compliance of \(\leq 50\) mol/cm H\(_2\)O; (5) the presence of bilateral chest radiograph infiltrates; and (6) appropriate risk for ARDS (Table 1). From February 1994 to March 1996, we identified ARDS patients by the presence of all of the following: (1) acute onset of lung injury requiring endotracheal intubation and mechanical ventilation; (2) P/F of \(\leq 173\) mm Hg (equivalent to 200 mm Hg at sea level); (3) bilateral chest radiograph infiltrates; (4) Pw of \(\leq 18\) mm Hg or no clinical evidence of left atrial hypertension; and (5) appropriate risk for ARDS (Table 1). From March 1996 to March 1999, we identified ARDS patients by the presence of all of the following: (1) acute onset of lung injury requiring endotracheal intubation and mechanical ventilation; (2) P/F of \(\leq 150\) mm Hg; (3) bilateral chest radiograph infiltrates; (4) total static thoracic compliance of \(\leq 50\) mol/cm H\(_2\)O; (5) the presence of bilateral chest radiograph infiltrates; and (6) appropriate risk for ARDS (Table 1).

We used the onset of ARDS as the temporal reference point for organ failure. We determined organ failure using the moderate dysfunction criteria from the Brussels organ failure scoring system for each patient for each day prior to the onset of ARDS and each day after its onset. We scored each organ failure daily as present or absent. An organ failure on any day prior to or after the onset of ARDS established organ failure as being present for the period prior to or after the onset of ARDS (Table 2). We evaluated sepsis using the severe dysfunction criteria of Montgomery et al11 for each day prior to the onset of ARDS and each day after its onset. The definition for sepsis was identical for both time periods. All data for scoring were collected prospectively and daily for all time points, and were stored in the database. APACHE (acute physiology and chronic health evaluation) II score was calculated prospectively, using the data from the first 24 h after the onset of ARDS. We used the lowest recorded Glasgow coma scale prior to intubation and/or after the patient was extubated to determine CNS failure.

We divided patients into the following two groups by year of ARDS onset: 1987 to 1990; and 1994 to 1999. We did not have complete data sets for 1990 to 1994 due to a temporary change in our research support. We therefore did not include the 1990 to 1994 patients. The oxygenation criterion for selecting ARDS patients in 1987 to 1990 used P(A-a)\(\text{O}_2\) ratio. The

<table>
<thead>
<tr>
<th>Organ Definition</th>
<th>Moderate Organ Dysfunction*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Systolic BP (\leq 90) mm Hg and unresponsive to fluids or receiving vasopressors</td>
<td></td>
</tr>
<tr>
<td>CNS, Glasgow coma score</td>
<td>(\leq 12)</td>
</tr>
<tr>
<td>Coagulation, (10^9) platelets/(\mu)L</td>
<td>(\leq 80)</td>
</tr>
<tr>
<td>Kidney, creatinine mg/dL</td>
<td>(\geq 2.0)</td>
</tr>
<tr>
<td>Liver, mg bilirubin/dL</td>
<td>(\geq 2.0)</td>
</tr>
</tbody>
</table>

*Taken from Bernard.10

**Table 1—ARDS Definition Used at LDS Hospital**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>P/F (\leq 150)</td>
<td>(\leq 105)</td>
<td>(\leq 150)</td>
<td>(\leq 173)</td>
</tr>
<tr>
<td>Pw, mm Hg</td>
<td>(\leq 15)</td>
<td>(\leq 18)</td>
<td>(\leq 18)</td>
</tr>
<tr>
<td>Cth, mL/cm H(_2)O</td>
<td>(\leq 50)</td>
<td>Not used</td>
<td>Not used</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>Bilateral infiltrates</td>
<td>Bilateral infiltrates</td>
<td>Bilateral infiltrates</td>
</tr>
<tr>
<td>Presence of risk factors</td>
<td>Required</td>
<td>Required</td>
<td>Required</td>
</tr>
</tbody>
</table>

*Cth = thoracic compliance.

†Represents the equivalent P/F for Pao\(_2\)/P\(\text{A0}_2\) \(\leq 0.2\).
subsequent publication of the North American-European Consensus Criteria led to the widespread adoption of a different and less severe set of criteria using a P/F criterion. In order to compare 1994-to-1999 patients with 1987-to-1990 patients, we established a correspondence between \( P(A-a)O_2 \) ratio and P/F (Fig 1). A P/F of \( \leq 105 \) corresponded to a \( P(A-a)O_2 \) of 0.2. In addition, for the 1994 to 1999 patients only, we compared patients identified with a P/F of 106 to 173 to those identified with P/F \( \leq 105 \).

We used death at the time of hospital discharge as the end point. We analyzed data by independent t test and Pearson \( \chi^2 \) analysis, and expressed the results as the mean \( \pm \) SEM.

**RESULTS**

We identified a total of 516 ARDS patients with a P/F of \( \leq 105 \) at ARDS onset (1987 to 1990, 256 patients; 1994 to 1999, 260 patients). We identified 288 patients (1994 to 1999) with a P/F range of 106 to 173.

A total of 548 ARDS patients (260 + 288) were identified between 1994 and 1999. Mortality was lower for those with higher arterial oxygenation efficiency (P/F, 106 to 173) than for those with lower arterial oxygenation efficiency (P/F, \( \leq 105 \)) [Table 3]. Between-group differences for age, gender, or risk factor for ARDS were not significant (Table 3).

Fewer total nonpulmonary organ failures were noted in 1994-to-1999 patients (Fig 3, with more patients having no and one organ failure, and fewer patients having two and three organ failures in 1994 to 1999 (p \( < 0.05 \)). Cardiovascular and CNS failure, and sepsis were significantly lower prior to ARDS onset (Fig 4) and after ARDS onset (Fig 5) among 1994-to-1999 patients. Hepatic failure was lower in the 1994-to-1999 patients only after ARDS onset (Fig 5).

Patients with higher arterial oxygenation efficiency (P/F, > 105) and those with lower arterial oxygenation efficiency (P/F, \( \leq 105 \)) in the 1994-to-1999 group had similar total nonpulmonary organ failure at ARDS onset (Fig 6) and similar distributions of organ failures both prior to ARDS onset (Fig 7) and after ARDS onset (Fig 8). In contrast, the 1987-to-1990 patients had a lower incidence of hepatic failure after ARDS onset, as ARDS evolved.
We found an inverse association between higher initial arterial oxygenation efficiency (i.e., P/F) and lower mortality (Fig 2, Table 3). This association of mortality with P/F was notably absent in the report of Zilberberg and Epstein. Their reported mortality rate was 58% both for patients with ALI and those with ARDS. However, their overall patient numbers were small, and they did not investigate mortality as a function of arterial oxygenation efficiency within the ARDS patient group. In addition, they studied only medical ICU patients, whereas we studied both medical and surgical patients.

We found an association between higher initial arterial oxygenation efficiency (i.e., P/F) and specific organ failure before and after ARDS onset (Figs 3–5, Table 3). The association of a greater incidence of organ failure in ARDS patients with a higher mortality is well-described and was observed in our 1994-to-1999 patients. However, the change in organ failure distribution that we observed has not been reported previously. A review of the literature (Table 4) demonstrated the paucity of reports of specific organ failures at or after the onset of ARDS. Bell et al. reported that increased organ failure occurring during ARDS was associated with increased mortal-

**Table 3—Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Dead</td>
<td>54</td>
<td>441†</td>
<td>271†</td>
<td>35†</td>
</tr>
<tr>
<td>Age, yr</td>
<td>54 ± 10</td>
<td>50 ± 11</td>
<td>52 ± 10</td>
<td>51 ± 10</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>48</td>
<td>55</td>
<td>57</td>
<td>56</td>
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<tr>
<td>APACHE II score</td>
<td>20 ± 7</td>
<td>20 ± 8</td>
<td>19 ± 8</td>
<td>20 ± 8</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>42</td>
<td>35</td>
<td>31</td>
<td>33</td>
</tr>
<tr>
<td>Sepsis</td>
<td>31</td>
<td>26</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Trauma</td>
<td>9</td>
<td>15</td>
<td>18*</td>
<td>17</td>
</tr>
<tr>
<td>Other</td>
<td>18</td>
<td>23</td>
<td>25</td>
<td>24</td>
</tr>
</tbody>
</table>

*Values given as % or mean ± SEM.
†p < 0.05 (compared with 1987–1990 patients).
‡p < 0.05.
ity. They found CNS, GI, renal, endocrine, and coagulation failure to be associated adversely with survival. Subsequent publications rarely have reported specific organ failures. Zilberberg and Epstein and the ARDS Network reported specific organ failures or the relation of mortality to specific

![Figure 3: Nonpulmonary organ failure for a P/F of ≤105 at ARDS onset for 1987-to-1990 and 1994-to-1999 patients. The horizontal axis represents the number of nonpulmonary organ failures. The numbers on the bar graphs are the total number of patients for that group.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22000/)

![Figure 4: Organ failure distribution for PaO2/FiO2≤105 vs. Time](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22000/)
organ failures. The evolution of organ failure following ARDS onset, and as a function of year of onset of ARDS, has not been reported systematically. In particular, longitudinal studies are lacking. APACHE II scores between the 1984-to-1990 and 1994-to-1999 patient groups were equivalent, so it is unlikely that group severity of illness was substantially different. The risk factors for the development

**Figure 5.** Organ failure distribution for a P/F of ≤105 after ARDS onset for 1987-to-1990 and 1994-to-1999 patients. See the legend of Figure 4 for abbreviations not used in the text. Numbers on the bar graphs are the total number of patients for that group.

**Figure 6.** Nonpulmonary organ failure at ARDS onset for 1994-to-1999 Patients vs P/F. The horizontal axis represents the number of nonpulmonary organ failures, and the numbers on the bar graphs are the total number of patients for that group.
of ARDS were not statistically different between the groups, but there was a nonstatistically greater percentage of pneumonia and sepsis (without significant changes in the contribution from trauma) in the earlier ARDS group. We recognize that the number of patients in this study may preclude finding a

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**Figure 7.** Organ failure distribution at ARDS onset for 1994-to-1999 patients vs P/F. See the legend of Figure 4 for abbreviations not used in the text. Numbers on the bar graphs are the total number of patients for that group.

**Figure 8.** Organ failure distribution after ARDS onset for 1994 to 1999 patients vs P/F. See the legend of Figure 4 for abbreviations not used in the text. Numbers on the bar graphs are the total number of patients for that group.
statistical difference in risk factors between the two groups that might be present, but this reinforces the necessity of reporting organ failure specifically in large future trials.

Unidentified cointerventions may have altered organ failure distribution and therefore have affected mortality. Therapy for critically ill patients has evolved. Examples of cointerventions that may have impacted ARDS are numerous, and include permissive hypercapnea, lowered airway pressure, and reduced tidal volume during mechanical ventilation. All of these could have reduced intrathoracic pressure and led to higher cardiac output. CNS blood flow might have increased and thereby preserved neurologic function. We recognize that animal and human evidence indicate that ventilatory strategies can be important in the genesis of cytokines that cause lung damage. However, we do not have adequate ventilatory data available to assess whether more recent ventilatory strategies are responsible for the changes we observed in organ failure distributions. Furthermore, our available data do not allow us to draw inferences regarding potential mechanisms of injury or repair. Until definitive data become available, any conclusions remain speculative.

We recognize that changes in care over time at our single center may not have reflected changes in care over time nationwide. However, many research centers have noted increased survival among ARDS patients, and the evidence suggests that mortality may have decreased since the 1970s. In addition, patients identified in the 1980s were identified using different criteria than those applied to patients in the 1990s. We accounted for this difference by comparing patients with similar oxygenation inefficiency criteria (ie, P/F).

Changes in organ failure distribution are a contributor in our environment to changes in mortality among ARDS patients. This observation may extend to the community at large. These observations of different organ failure distributions associated with different mortality rates among ARDS patients from 1987 to 1990 and from 1994 to 1999 emphasize the need for rigorous experimental design and reporting in future ARDS clinical investigations.

**REFERENCES**

9. Pryor TA. The HELP medical record system. MD Comput 1988; 5:22–33

**Table 4—Previous ARDS Reports With Organ Failure**

<table>
<thead>
<tr>
<th>Study-Year</th>
<th>Patients, No.</th>
<th>ICU Type</th>
<th>APACHE II Score</th>
<th>Before ARDS Onset</th>
<th>After ARDS Onset</th>
<th>Organ Failure Distribution Reported</th>
</tr>
</thead>
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<tr>
<td>Bell$^{1/2}$/1983</td>
<td>141</td>
<td>Mixed</td>
<td>NA</td>
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<td>Montgomery$^{1/2}$/1985</td>
<td>207</td>
<td>Mixed</td>
<td>NA</td>
<td>No</td>
<td>No</td>
<td>Cause of death</td>
</tr>
<tr>
<td>Millberg$^{1}$/1995</td>
<td>918</td>
<td>Mixed</td>
<td>NA</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Doyle$^{1}$/1995</td>
<td>57</td>
<td>Mixed</td>
<td>NA</td>
<td>No</td>
<td>Multiple linear regression</td>
<td>No</td>
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<tr>
<td>Zilberberg and Epstein$^{2}$/1998</td>
<td>81</td>
<td>Med</td>
<td>19</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Abel$^{1}$/1998</td>
<td>120</td>
<td>Mixed</td>
<td>14</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>ARDS Network$^{16}$/2000</td>
<td>1832</td>
<td>Mixed</td>
<td>S1$^+$</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>ARDS Network$^{17}$/2000</td>
<td>861</td>
<td>Mixed</td>
<td>S2$^+$</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

*NA = not applicable.
†APACHE III score.

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