Improved Survival in Patients with AIDS, 
Pneumocystis carinii Pneumonia, and 
Severe Respiratory Failure*

Yaakov Friedman, M.D.; Cory Franklin, M.D.; 
Eric C. Rackow, M.D., F.C.C.P.; and Max Harry Weil, M.D., F.C.C.P.

Pneumocystis carinii pneumonia (PCP) causing acute respiratory failure (ARF) in patients with acquired immunodeficiency syndrome (AIDS) has been reported in several studies to have a mortality of 84 to 100 percent. A recent report found a 42 percent survival rate. We followed 58 patients with AIDS who required positive pressure ventilation and identified 33 patients with PCP and ARF who had a PaO₂/FIO₂ level <150 mm Hg. We report the survival of 12 of these 33 (36 percent). The mean duration of survival after discharge from the hospital was 7.9 ± 1.8 months, which is an improvement over previous reports. These data suggest that we should reevaluate the reported recommendations that patients with AIDS, PCP and ARF should not receive intensive care or mechanical ventilation.

(Chest 1989; 96:862-66)

Since recognition of the acquired immunodeficiency syndrome (AIDS) in 1981, there have been 82,764 cases reported in the United States (Centers for Disease Control, [CDC] personal communication, January, 1989). Approximately 45 percent of the patients develop pulmonary disorders, including infection, nonspecific inflammation and cancer. In these patients, mortality for each episode is 41 percent.1,2

Pneumocystis carinii pneumonia (PCP) is the most common opportunistic infection involving the lungs, occurring in 50 to 85 percent of patients with pulmonary problems.1,3 The mortality of a single episode of PCP is 28 to 43 percent.2,4

Acute respiratory failure (ARF) is a common sequela in patients with AIDS and PCP. The mortality of patients with AIDS, PCP and ARF previously has been reported to be 84 to 100 percent.1,2,4,9 To confirm our impression of increased survival of these patients in our intensive care unit, we undertook a prospective study.

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METHODS

We followed the course of all patients admitted to the Medical Intensive Care Unit with AIDS, who required positive pressure ventilation, from January 1, 1987 through December 31, 1988. AIDS was defined according to CDC criteria as the presence of an opportunistic infection or Kaposi’s sarcoma in a person under 60 years who has no underlying immunsuppressive disease and has not received immunosuppressive therapy.10 ARF was defined as a PaO₂ less than 60 mm Hg while breathing a gas mixture of at least 40 percent oxygen or an equivalent PaO₂/FIO₂ ratio less than 150 mm Hg.11 Positive pressure ventilation was administered with either continuous positive airway pressure (CPAP) by mask or endotracheal intubation and mechanical ventilation.

All patients underwent diagnostic fiberoptic bronchoscopy with bronchoalveolar lavage and/or transbronchial biopsy. The diagnosis of PCP was established with identification of cysts by silver methenamine stains or trophozoites by Giemsa stain.

Demographic data including age, sex, race, and risk factors for the development of AIDS were collected. We also recorded the reason for admission to the Intensive Care Unit, length of diagnosis of AIDS prior to admission, previous episodes of PCP, number of days in hospital prior to initiation of positive pressure ventilation, interval between bronchoscopy and positive pressure ventilation, PCP/FIO₂ ratio at time of Intensive Care Unit admission and prior to positive pressure ventilation, duration of positive pressure ventilation, maximum positive end-expiratory pressure (PEEP) or CPAP, other infections, complications, procedures performed, antibiotic therapy, duration of Intensive Care Unit stay, and duration of hospital stay.

Patients were observed through their entire hospital course, with survival defined as discharge from hospital. All survivors were followed after their hospital discharge.

Data are expressed as the mean ± SEM. The chi-square test and Student t-test were used to assess the significance of differences between groups. A p value less than 0.05 was considered statistically significant.

RESULTS

During the study period, 58 patients with AIDS who required positive pressure ventilation were admitted to the Medical Intensive Care Unit. Thirty-three patients were identified as having PCP and ARF. There were two patients with AIDS and PCP who were admitted for renal failure and required mechanical ventilation for worsening metabolic acidosis and fluid overload. Twenty patients were placed on mechanical ventilation for ARF of other etiologies including mycobacterial disease, Kaposi’s sarcoma, disseminated fungal disease, sepsis, or neurologic disease requiring airway protection. We were unable to establish a diagnosis in three patients who were admitted for ARF.
Table 1—Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Survivors (n = 12)</th>
<th>Non-Survivors (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>36</td>
<td>64</td>
</tr>
<tr>
<td>Age (median)</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>Age (range)</td>
<td>25-54</td>
<td>21-55</td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>White</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Black</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Risk Factors

Homosexual  
Intravenous drug abuser  
Heterosexual

Twelve of the 33 patients (36 percent) with PCP and ARF were discharged from the hospital. The characteristics of these patients are listed in Table 1. Two survivors were both homosexuals and intravenous drug users. Eleven of the survivors (92 percent) and 16 of the nonsurvivors (76 percent) had newly diagnosed AIDS. One survivor was diagnosed to have AIDS with PCP that did not result in ARF nine months prior to admission. Five of the nonsurvivors had AIDS for three, four, seven, ten and 12 months respectively. Two of the nonsurvivors had previous episodes of PCP, which did not result in ARF. One of the nonsurvivors had survived an episode of PCP and ARF 12 months prior to admission. The number of patients with prior episodes of PCP and ARF is too small to draw any conclusions regarding survival.

Indices of the severity of illness and ARF are shown in Table 2. The patient who required only CPAP support had a PaO2/FIO2 ratio of 106 prior to initiation of positive pressure ventilation. Five survivors (42 percent) and three non-survivors (5 percent) were initially supported with CPAP but needed endotracheal intubation after one to eight days due to worsening ARF. Nine out of 12 survivors (75 percent) and 15 of 21 (71 percent) nonsurvivors were placed on positive pressure ventilation within five days of hospitalization (NS).

Table 2—Severity of Acute Respiratory Failure

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubated</td>
<td>11</td>
<td>21</td>
</tr>
<tr>
<td>CPAP</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Days prior to positive pressure ventilation</td>
<td>4.2 ± 0.6</td>
<td>5.7 ± 1.1</td>
</tr>
<tr>
<td>Duration of positive pressure ventilation (days)</td>
<td>13.4 ± 3.4</td>
<td>16.4 ± 2.2</td>
</tr>
<tr>
<td>Days in intensive care unit</td>
<td>19.8 ± 3.2</td>
<td>19.0 ± 2.8</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>34.9 ± 4.2</td>
<td>27.5 ± 3.8</td>
</tr>
<tr>
<td>PaO2/FIO2 prior to positive pressure ventilation</td>
<td>80.2 ± 6.0</td>
<td>78.1 ± 7.1</td>
</tr>
<tr>
<td>Maximum PEEP cm H₂O</td>
<td>10.8 ± 1.5</td>
<td>18.2 ± 1.4*</td>
</tr>
</tbody>
</table>

Mean ± SE  
*p<0.05

Four survivors (33 percent) and seven nonsurvivors (33 percent) were intubated prior to bronchoscopy. Three survivors (25 percent) and eight nonsurvivors (38 percent) needed positive pressure ventilation within 24 hours after undergoing fiberoptic bronchoscopy. The remaining five survivors (42 percent) and five nonsurvivors (24 percent) were intubated more than 24 hours after bronchoscopy. No significant difference was observed in survival when comparing those patients intubated prior to or after bronchoscopy. In addition, there was no significant difference in survival between those patients intubated less than or more than 24 hours after bronchoscopy. Positive pressure ventilation was initiated 2.3 ± 0.6 days after bronchoscopy in the survivors and 4.3 ± 1.6 days in the nonsurvivors (NS).

The antibiotic therapy received by the patients is shown in Table 3. All patients were initially treated with trimethoprim-sulfamethoxazole unless there was a history of prior hypersensitivity. All but two patients eventually had their antibiotics changed either due to treatment failure or toxicity. All changes in the patient’s antibiotic regimen were made at the discretion of the attending physician based on the patient’s clinical condition. There was no statistical difference in survival based on the treatment received. Five of 12 survivors (42 percent) and five of 21 nonsurvivors (24 percent) received steroids during their hospital course (NS).

Two survivors had additional pulmonary opportunistic infections: Candida and Mycobacterium tuberculosis. One survivor had cytomegalovirus retinitis. Five nonsurvivors had additional pulmonary opportunistic infections. Two patients had disseminated Candida, two patients had herpes simplex virus, and one patient had cytomegalovirus and Hemophilus influenzae. One nonsurvivor had Cryptosporidium in his stool. One nonsurvivor had a Pseudomonas urinary tract infection. There was no significant difference in the incidence of other opportunistic infections between the survivors and nonsurvivors.

Table 3—Therapy for PCP

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP/SMX → pentamidine</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>TMP/SMX → pentamidine → DFMO</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>TMP/SMX → pentamidine + steroids</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Pentamidine → DFMO</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>TMP/SMX → pentamidine → TMP/dapsone + steroids</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>TMP/SMX → pentamidine → DFMO → TMP/dapsone + steroids</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Pentamidine → TMP/dapsone</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>TMP/SMX + steroids</td>
<td>2</td>
<td>—</td>
</tr>
</tbody>
</table>

TMP = trimethoprim; SMX = sulfamethoxazole; DFMO = alpha difluoromethylornithine

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Two survivors (17 percent) and six nonsurvivors (29 percent) developed pneumothoraces which necessitated the placement of thoracostomy tubes. Four survivors (33 percent) and 17 nonsurvivors (81 percent) had pulmonary artery catheters inserted for hemodynamic monitoring. Two nonsurvivors underwent hemofiltration for renal failure and fluid overload.

Four of the nonsurvivors were initially weaned from positive pressure ventilation and discharged from the Intensive Care Unit. One patient was readmitted after suffering cardiopulmonary arrest secondary to hypoglycemia caused by the administration of pentamidine. Two other patients were readmitted with recurrent ARF and positive pressure ventilation was re instituted. The length of positive pressure ventilation and Intensive Care Unit stay were combined for both of these patients’ admissions to the Intensive Care Unit. The final patient was extubated and discharged from the Intensive Care Unit. He then developed candidemia and staphylococcal sepsis. He refused reintubation and died of ARF.

All survivors were observed after discharge (Table 4). Two survivors were lost to follow-up, one at three months and one at six months after discharge. Three patients have died from 5.5 months to 13.5 months after their initial hospital discharge. The other seven patients are alive from 0.5 months to 16 months after discharge. Of the ten patients where follow-up is available, the mean survival was 7.9±1.8 months. Forty weeks (11 percent) of their time after discharge was spent in the hospital.

**DISCUSSION**

Patients with AIDS and PCP who develop ARF requiring mechanical ventilation were previously reported to have a survival of 0 to 16 percent, with a composite survival of 27 of 224 patients (12 percent). This has led to the belief that patients with PCP who develop ARF would not benefit from aggressive Intensive Care Unit intervention including intubation and positive pressure ventilation. Rosen et al stated that “it is clear that most patients with AIDS who develop respiratory failure would benefit maximally by not undergoing mechanical ventilation or other invasive therapies.” In a recent study comparing trimethoprim-sulfamethoxazole and pentamidine for the treatment of PCP, the decision whether a patient would be placed on mechanical ventilation was “usually discouraged by the investigators and physicians caring for the patients.” Although a study found that 55 percent of homosexual males with AIDS wanted admission to the Intensive Care Unit and mechanical ventilation, the suggestion was made that patient education and counseling regarding the poor prognosis would lead patients to decide against such treatment. As a result, there has been a decrease in the percentage of hospitalized patients with AIDS who are admitted to the Intensive Care Unit. The possibility exists that institutions that discourage admission of patients with PCP and ARF will not see improving survival, creating a self-fulfilling prophecy. We undertook this study to document our impression that survival is increasing in patients with AIDS and PCP who develop ARF.

The survival rate of 36 percent in our study is in agreement with a recent study which reported a 42 percent survival rate in patients with AIDS and PCP who required mechanical ventilation. However, seven of their eight survivors were placed on mechanical ventilation because of deterioration in their respiratory status soon after bronchoscopy, as opposed to nine of their 11 nonsurvivors who required mechanical ventilation.
ventilation unrelated to bronchoscopy. In our patients, there was no significant relationship between the interval from bronchoscopy to positive pressure ventilation and survival. Although eight of 12 survivors were intubated after bronchoscopy, only three deteriorated within 24 hours. This makes hypoxia induced by bronchoscopy less likely as a cause of ARF.

In our study, the only identifiable difference between the survivors and nonsurvivors was that the maximum PEEP utilized was higher in the nonsurvivors. This was most likely related to continued respiratory deterioration in the nonsurvivors, who thus needed increasing amounts of ventilatory support.

As both trimethoprim-sulfamethoxazole and pentamidine are accepted as efficacious for the treatment of PCP, these drugs were used as initial therapy. Patients who had treatment failure, as determined by the attending physician, or developed toxicity were treated with other drugs. These included alpha-defluoromethoxilnithine, trimethoprim/dapsone, and steroids. We were unable to demonstrate any difference in survival based on type of therapy.

The reason for the improved survival in our patients compared to that of previous reports is unclear. PCP in AIDS patients has been shown to present in a more insidious fashion with less tachypnea and hypoxia than PCP occurring in other immunosuppressed patients. The course of PCP has been shown to be similar to the adult respiratory distress syndrome in both renal transplant patients and patients with AIDS. Thus, patients who present later in the course of the disease would tend to have more pulmonary fibrosis and decreased likelihood of survival. With the increased awareness of the symptoms of PCP by patients with AIDS, it is likely that they are seeking medical attention earlier in the course of the disease. This was one of the factors that was found to be different between the survivors and nonsurvivors in the study by El-Sadr et al.

Our observations may reflect a learning curve, as was suggested in a previous report that found a significant improvement in the one-year probability of survival in AIDS patients with PCP. Six patients have not had subsequent hospitalizations. One patient was only in the hospital for a total of 2.5 weeks in the 13 months between his initial discharge and final admission. While quality of life is difficult to measure, all survivors except one were discharged home and functioned normally, returning regularly for clinic follow-up. The survivor who recovered from coma was initially discharged to a rehabilitation facility. It is interesting to note that the survival rate in our patients is the same as that reported by Kovacs et al in patients with PCP who are immunosuppressed for reasons other than AIDS.

Recent reports show a beneficial effect of steroids on survival in AIDS patients with PCP who develop ARF. Though there was no statistical difference in our patients who did and did not receive steroids, the only two patients who did not require a second antibiotic received steroids as soon as they developed ARF. There was also an improved one-year survival in patients with AIDS and PCP in New York since 1985, and a decreased frequency of opportunistic infections and improved survival in patients receiving azidothymidine. Newer therapies for PCP such as alphadefluoromethoxilnithine, trimethoprim/dapsone, trimetrexate, and inhaled pentamidine may be of potential benefit.

In summary, we observed an improved survival in patients with AIDS and PCP who develop ARF. In light of our findings, we believe that competent patients should be allowed to make well-informed choices regarding intensive care, intubation and mechanical ventilation. Furthermore, we believe that optimism is warranted during discussions with patients regarding these decisions.

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