CD4 Lymphocyte Counts and Mortality in AIDS Patients Requiring Mechanical Ventilator Support due to Pneumocystis carinii Pneumonia*

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**Objective:** To evaluate CD4 counts as a predictor of mortality in AIDS patients with respiratory failure due to *Pneumocystis carinii* pneumonia (PCP).

**Design:** Retrospective chart review.

**Setting:** Urban university medical center.

**Patients:** Forty-eight patients admitted to the medical ICU from January 1993 to August 1996 with diagnosis of HIV/AIDS, PCP, CD4 count <200 cells per cubic millimeter, who required mechanical ventilation for respiratory failure.

**Interventions:** Medical records were reviewed and age, CD4 count, lactate dehydrogenase, room air (RA) PaO₂, coinfections, and day of admission to day of intubation (DOA-D0I) data were recorded.

**Results:** All 48 patients (12 women and 36 men) were treated with corticosteroids and IV trimethoprim-sulfamethoxazole. Age ranged from 21 to 65 years; CD4, 1 to 180, RA PaO₂, 27 to 93 mm Hg; and DOA-D0I, 0 to 20 days. Mortality varied significantly depending on CD4 counts: CD4 0 to 10 (100%); CD4 11 to 50 (88%); CD4 51 to 100 (50%); and CD4 >100 (25%). There were no significant difference in mortality between the groups with DOA-D0I <5 days (82%) vs >5 days (80%) or between the groups with PaO₂ <60 mm Hg (85%) vs PaO₂ >60 mm Hg (73%).

**Conclusion:** Even though overall mortality was 81%, the mortality rate was significantly different among the four groups. Most striking was the progressive increase in mortality as CD4 cells decreased from >100 (25% mortality) to <10 (100% mortality). Survivors had significantly higher CD4 cell counts than those who died. The CD4 cell count within 2 weeks of admission has significant prognostic value and may be helpful when counseling patients, families, and healthcare surrogates in end-of-life decision making.

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**Key words:** lymphocytes; mechanical ventilation; *Pneumocystis carinii* pneumonia; respiratory failure

**Abbreviations:** DOA-D0I=day of admission to day of intubation; LDH=lactate dehydrogenase; MVS=mechanical ventilator support; PCP=*Pneumocystis carinii* pneumonia

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Patients with AIDS who require ICU admission for *Pneumocystis carinii* pneumonia (PCP) present a difficult challenge in care and management. Predicting outcomes has been difficult in this group of patients when they develop respiratory failure due to PCP. When mechanical ventilator support (MVS) is required, mortality is excessively high. Many different parameters have been examined in an attempt to predict the outcome of AIDS patients with PCP. Knowledge of outcome determinants can be helpful in assessing the immediate risk of acute deterioration as well as predicting long-term prognosis. Before selecting a course of therapy, patients and families expect physicians to be able to provide an assessment of the patient’s chances of survival and quality of life. Outcome analysis can assist in these decisions.

Many studies over the past 15 years have examined various factors to determine ICU mortality for PCP and respiratory failure in AIDS patients. Results from these investigations have been inconsistent, even when the same parameters were studied. CD4 lymphocytes are important regulators in the immune system. Depletion of CD4 cells plays an integral role in the pathogenesis and progression of AIDS. Although CD4 counts have been incorporated into mortality evaluations, to our knowledge, no studies published in the English-language literature have
focused on the range of CD4 counts in predicting ICU mortality in AIDS patients with respiratory failure due to PCP. Therefore, we reviewed the records of 45 patients to determine the value of the CD4 count along with age, lactate dehydrogenase (LDH), day of admission to day of intubation (DOA-D01), and PaO2 in predicting mortality from respiratory failure in patients with AIDS who required MVS because of PCP.

**MATERIALS AND METHODS**

**Subjects**

The medical records of all patients who were admitted to a city university teaching hospital from January 1993 to August 1996 with the diagnosis of mechanical ventilation along with HIV, AIDS, and PCP were retrospectively reviewed. Because this involved only chart review, no informed consents were required. The inclusion criteria for further analysis of data were as follows: (1) age 18 years or older; (2) confirmed diagnosis of HIV infection and AIDS; (3) confirmed diagnosis of PCP by BAL or biopsy specimen; (4) intubation and MVS due to respiratory failure due to PCP; (5) CD4 count <200 cells per cubic millimeter obtained within 2 weeks before or after the institution of MVS; and (6) no other major medical problems or multiorgan failure on admission. Forty-eight patients met all criteria and constituted the study population. There were 36 men and 12 women. No concomitant infections were noted on BAL or biopsy specimens in any of the cases. All patients had been treated with corticosteroids and IV trimethoprim-sulfamethoxazole. Three patients were subsequently switched to IV pentamidine due to clinical deterioration.

The 45 patients were divided into four groups based on their CD4 count: group 1, 0 to 10 cells per cubic millimeter (n=20); group 2, 11 to 50 cells per cubic millimeter (n=16); group 3, 51 to 100 cells per cubic millimeter (n=8); and group 4, 101 to 200 cells per cubic millimeter (n=4). Age, CD4 count, serum LDH, PaO2 while breathing room air, and DOA-D01 were recorded for each patient. Nine patients recovered from their episode of PCP and were discharged from the hospital (survivors). Thirty-nine patients died during their hospitalization due to complications of PCP (nonsurvivors). The patients were also analyzed based on DOA-D01 ≤5 days vs >5 days and on PaO2 ≤60 mm Hg vs >60 mm Hg.

**Statistical Methods**

Values are expressed as mean±SD. Statistical analyses were done using a computer-based package (Systat Inc; Evanston, Ill). Student’s t test was used for comparison between survivors and nonsurvivors. Analysis of variance was used for testing significance among groups 1 to 4 and Tukey’s procedure was used to correct for analysis of multiple groups.5 Mortality rate comparisons between patients with PaO2 ≤60 vs >60 mm Hg and patients with DOA-D01 ≤5 days vs >5 days were made using Fisher’s Exact Test. A p value ≤0.05 was considered statistically significant.

**RESULTS**

There were no statistical differences among groups 1 to 4 in terms of age, LDH, PaO2, and DOA-D01. However, mortality rate was significantly different among the groups based on CD4 cell counts (Fig 1). Although the inclusion criteria allowed for patients to be entered into the study if a CD4 count <200 cells per cubic millimeter was obtained within 2 weeks before or after MVS, all the CD4 counts in this study were obtained prior to or on the day that MVS was begun. Most of the cell counts (77%) were obtained within 72 h of commencing MVS and 94% within 1 week (Fig 2).

Thirty-nine patients (81%) died (nonsurvivors) and 9 patients survived (survivors). The characteristics of the survivors and nonsurvivors are listed in Table 1. There were no statistical differences between the two groups in terms of LDH, PaO2, and DOA-D01. CD4 lymphocytes were significantly lower in the nonsurvivor group (Table 1).

There was no significant difference in mortality between the group with DOA-D01 ≤5 days (31/38, 82%) compared to the group with DOA-D01 >5 days (8/10, 80%). Similarly, no statistical difference was found when comparing the mortality in the 33 patients who presented with PaO2 ≤60 mm Hg (85%) to the 15 patients who presented with PaO2 >60 mm Hg (73%).

**DISCUSSION**

PCP is a major cause of respiratory failure in patients with the AIDS.6 Initial data from the early 1980s reported 80 to 100% mortality rates for AIDS patients requiring MVS for PCP.6-10 Reports of ICU outcomes after 1986 showed improved survival11-14 that was partly attributed to the adjunctive use of corticosteroids.11,12,15 Other factors that may have contributed to the decrease in mortality include a better knowledge of this opportunistic infection, an improvement in diagnostic methods, more wide-
spread use of PCP prophylaxis, and the introduction of zidovudine in 1986.16,17 Unfortunately, the most recent data suggest an increased mortality in AIDS patients who require mechanical ventilation for acute respiratory failure complicating PCP infection.15,18,19

The absolute number of circulating CD4 lymphocytes is a clinically useful indicator of immune function in patients infected with HIV and can be used to stratify patients according to severity of illness.20 A poor short-term prognosis was noted by Yarchoan and colleagues4 when the CD4 count was <50 cells per cubic millimeter. When they evaluated 55 patients who received antiretroviral therapy at an advanced stage of disease, no deaths occurred unless the CD4 counts were <50 cells per cubic millimeter. Easterbrook et al21 confirmed this observation in a larger cohort of zidovudine-treated patients.

In the present study, the mortality rate for patients who required MVS due to respiratory failure from PCP and had CD4 counts <50 cells per cubic millimeter was 94% (Table 2). Even more striking was the progressive increase in mortality rate as the CD4 counts declined from >100 cells (25%) to ≤10 cells per cubic millimeter (100%) (Fig 1). De Palo et al15 evaluated ICU outcome in HIV-infected patients and found a mortality rate of 81% in patients with PCP and respiratory failure who required MVS despite adjunctive corticosteroid therapy. They noted a relationship among respiratory failure, mortality, and declining CD4 lymphocyte count. Only 16 of their patients had PCP and respiratory failure, of whom 13 died (81% mortality). No further conclusions concerning CD4 counts and mortality in this specific group of patients could be made.

In the mid-1980s, investigators in Miami,10 San Francisco,7 and New York6 noted that survival after respiratory failure in patients with AIDS was ≤15%. Over the next few years, various prognostic parameters were examined in an effort to predict mortality. The APACHE (acute physiology and chronic health evaluation) II classification incorporates 12 physiologic variables in a schema designed to predict mortality. When applied to a subgroup of 37 patients with HIV and PCP who required MVS, the observed mortality (87%) was twice the predicted rate (44%).8 Peruzzi et al18 analyzed multiple physiologic, laboratory, and radiographic parameters in a group of 27 patients with HIV, PCP, and MVS. No parameter at the time of admission was significant in predicting mortality. The only statistically significant parameters that differed between survivors and nonsurvivors are listed in Table 1 and Table 2.

### Table 1—Survivors vs Nonsurvivor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Nonsurvivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>Age, yr</td>
<td>37.8±9.9</td>
<td>41.6±11.4</td>
</tr>
<tr>
<td>Female:Male</td>
<td>3.6</td>
<td>9:30</td>
</tr>
<tr>
<td>CD4 counts, cells/mm³</td>
<td>51.3±15.7</td>
<td>23.5±31.0</td>
</tr>
<tr>
<td>LDH, U</td>
<td>1,510±1,133</td>
<td>1,923±988</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
<td>62.2±18.4</td>
<td>52.7±14.4</td>
</tr>
<tr>
<td>DOA-DOI, d</td>
<td>3.9±3.1</td>
<td>3.9±5.4</td>
</tr>
</tbody>
</table>

*p<0.02 compared to nonsurvivors.

### Table 2—Characteristics of Groups Based on CD4 Counts

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>20</td>
<td>16</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Age, yr</td>
<td>41.5±11</td>
<td>38.2±8</td>
<td>38.8±11</td>
<td>47.5±14</td>
</tr>
<tr>
<td>Female:Male</td>
<td>9:15</td>
<td>3:13</td>
<td>3:5</td>
<td>1:3</td>
</tr>
<tr>
<td>CD4 counts, cells/mm³</td>
<td>2,032±1,159</td>
<td>2,621±764</td>
<td>2,296±1,180</td>
<td>1,119±238</td>
</tr>
<tr>
<td>LDH, U</td>
<td>2,032±1,159</td>
<td>1,621±764</td>
<td>2,296±1,180</td>
<td>1,119±238</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
<td>51.3±15.7</td>
<td>58.0±13.5</td>
<td>56.5±17.5</td>
<td>52.8±20.8</td>
</tr>
<tr>
<td>DOA-DOI, d</td>
<td>2.9±5.8</td>
<td>4.9±5.6</td>
<td>4.3±6.7</td>
<td>4.5±4.7</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>100</td>
<td>50</td>
<td>85</td>
<td>25</td>
</tr>
</tbody>
</table>

*Group 1, CD4 count, ≤10 cells per cubic millimeter; group 2, CD4 count, 11 to 50 cells per cubic millimeter; group 3, CD4 count, 51 to 100 cells per cubic millimeter; group 4, CD4 count, 101 to 200 cells per cubic millimeter.

1No statistically significant differences among groups 1 to 4.
were the presence of a metabolic acidosis at any time during the hospitalization and the requirement for a positive-end-expiratory pressure level >10 cm H2O after 4 days in the ICU. However, CD4 lymphocytes were not reported in their study. Similarly, Efferen et al12 were unable to identify clinical or laboratory data that predicted survival, although they noted a decline in LDH levels in patients who survived. The LDH levels in the patients who survived in the present study were higher than nonsurvivors, but this difference was not statistically significant (Table 1). Another factor that has been associated with worse outcome is poor oxygenation. The PaO2 in nonsurvivors in this study was lower than in the survivors (Table 1) but was not predictive of outcome. Since both groups had severe enough conditions to require MVS, their baseline oxygenation was already poor and therefore not discriminatory.

Staikowsky et al19 observed that the mortality rate of 33 patients with AIDS, PCP, and respiratory failure was significantly higher (100% vs 50%) when MVS was required ≥5 days after initiation of treatment for PCP with corticosteroids and antimicrobial therapy compared to patients who were intubated for MVS within the first 48 h. No other physiologic parameter studied was statistically predictive. In the present study, there was no difference in mortality in the 38 patients who were given MVS ≤5 days after admission (82%) compared to the patients intubated for MVS later during their hospitalization (80%).

Realizing the enormous emotional and economic impact that caring for patients with a poor prognosis for survival has on health-care providers and the health-care system,6 various authors have recommended research aimed at determining better prognostic indicators of outcome in this group of patients.14,15 Based on the data presented in this study, the CD4 lymphocyte count within 1 week prior to the institution of MVS for PCP-related respiratory failure in a patient with AIDS appears to have significant prognostic value and may be helpful when counseling patients, families, and health-care surrogates in end-of-life decision making. However, the design of this report allowed only a demonstration of a significant correlation between a specific laboratory value and mortality rates. A prospective validation study will be necessary to calculate the diagnostic accuracy of the CD4 lymphocyte count as a predictor of mortality in this group of patients.

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REFERENCES


