Outcome From Mechanical Ventilation After Autologous Peripheral Blood Stem Cell Transplantation*

Basheer Y. Khassawneh, MD; Peter White, Jr., MD; Elias J. Anaissie, MD, PhD; Barthel Barlogie, MD, PhD; and F. Charles Hiller, MD, FCCP

**Study objective:** To report the outcome of patients with autologous peripheral blood stem cell transplantation (PBSCT) receiving mechanical ventilation.

**Design:** Retrospective observational study.

**Setting:** Active hematopoietic stem cell transplantation center and a university hospital medical ICU.

**Patients:** Patients with autologous PBSCT receiving mechanical ventilation.

**Method:** A review of the medical records of patients with autologous PBSCT receiving mechanical ventilation. Data collection was restricted to the first episode of mechanical ventilation.

**Results:** A total of 78 autologous PBSCT patients received mechanical ventilation for >24 h. Twenty patients (26%) were extubated and discharged alive from the hospital. Thirteen hospital survivors (60%) were alive at 6 months. Lung injury (LI), vasopressor use, and hepatic and renal failure (HRF) were used to predict survival after mechanical ventilation. Sixty patients (76%) had no organ failure, or had isolated LI or only required treatment with vasopressors. Their hospital survival and 6-month survival were 32% and 20%, respectively. Hospital and 6-month survival for the patients with HRF or LI and vasopressor use was 6% and 0%, respectively.

**Conclusions:** Prolonged mechanical ventilation and aggressive ICU support is justified for autologous PBSCT patients receiving mechanical ventilation with no organ failure, or who have only isolated LI, or who only require treatment with vasopressors.

(CHEST 2002; 121:185–188)

**Key words:** autologous transplantation; bone marrow transplantation; hematopoietic stem cell transplantation; mechanical ventilators; multiple myeloma; multiple organ failure; outcome assessment; respiratory insufficiency; survival

**Abbreviations:** BMT = bone marrow transplant; HPSCT = hematopoietic stem cell transplantation; HRF = hepatic and renal failure; LI = lung injury; PBSCT = autologous peripheral stem cell transplantation; UAMS = University of Arkansas for Medical Sciences

Hematopoietic stem cell transplantation (HPSCT) is standard therapy for numerous malignant and nonmalignant disorders, and it can be curative. Transplanted stem cells can be obtained from bone marrow or peripheral blood. Historically, hospital or 30-day survival for bone marrow transplant (BMT) patients who required mechanical ventilation for respiratory failure was very low (4 to 13%).2–12 These studies prompted some to question the routine use of mechanical ventilation for respiratory failure in BMT patients.13,14 Autologous peripheral blood stem cell transplantation (PBSCT) accounts for approximately 60% of all HPSCT.15,16 The outcome of respiratory failure requiring mechanical ventilation for patients with autologous PBSCT has not been widely reported.11

The University of Arkansas for Medical Sciences (UAMS) has an active HPSCT program for patients with multiple myeloma.17,18 Approximately 300 transplants are performed each year. Eighty-five percent of these transplants are for multiple myeloma, and 80% are for autologous PBSCT. The purpose of this study was to describe the outcome for patients receiving mechanical ventilation after autologous PBSCT at UAMS.

**Materials and Methods**

This was an observational study. All patients who received autologous PBSCT at UAMS between March 1, 1991, and April
30, 1999, were eligible for the study. The UAMS Human Research Advisory Committee approved the study.

Autologous PBSCT patients with acute respiratory failure requiring mechanical ventilation were transferred to the university hospital medical ICU, a closed ICU where patients are cared for by the pulmonary and critical care staff and fellows, and the internal medicine house staff. These patients were seen regularly by the marrow transplant team.

Data were collected from the first episode of mechanical ventilation after autologous PBSCT. If a patient had more than one episode of mechanical ventilation, only data from the first episode were collected. The medical records of these patients were reviewed; age, gender, transplant date, underlying diagnosis, duration of mechanical ventilation, status at discharge, and date of death or last contact were recorded. The highest values of fraction of inspired oxygen and positive end-expiratory pressure for the period between 24 h and 72 h after initiation of mechanical ventilation were recorded.⁹

Mechanical ventilation was defined as endotracheal intubation and positive-pressure ventilation for ≥ 24 h. Hospital survival was defined as extubation and discharge alive from the hospital. BMT was HPSCT utilizing stem cells harvested from bone marrow. PBSCT was HPSCT utilizing stem cells harvested from peripheral blood.

The conditioning regimen for the autologous PBSCT patients included melphalan, 140 to 200 mg/m² with or without cyclophosphamide, 1.25 g/m², or total body irradiation, or BEAM (carmustine, 300 mg/m²; etoposide, 200 mg/m²/d for 3 days; cytarabine, 400 mg/m²/d for 4 days; and melphalan, 140 mg/m²).² Stem cell infusion (CD-34 > 1 × 10⁶/kg) was usually administered IV 24 h after the conditioning regimen.¹⁹ All patients received prophylactic antibacterial (oral quinolone), antiviral (acyclovir), and antifungal agents (fluconazole) from the initiation of their chemotherapy until recovery of neutrophils (> 1,000/µL). Neutropenic fevers were treated with broad-spectrum antibiotics with the addition of amphotericin B as clinically indicated.

The definition for organ failure was based on the method of Rubenfeld and Crawford.² The use of vasopressors, a surrogate for hemodynamic instability, was the administration of dopamine, > 5 µg/kg/min, or any use of norepinephrine, epinephrine, or phenylephrine for > 4 h during the first 72 h of mechanical ventilation. Hepatic and renal failure (HRF) was a total serum bilirubin level > 4 mg/dL and a serum creatinine level > 2 mg/dL during the initial 72 h of mechanical ventilation. Lung injury (LI) was a fraction of inspired oxygen > 0.6 and/or positive end-expiratory pressure > 5 cm H₂O between 24 h and 72 h of the initiation of mechanical ventilation. No organ failure was the absence of LI, no vasopressor use, and the absence of HRF during the initial 72 h of mechanical ventilation. Oligo-organ failure was defined as LI or vasopressor use. Two-organ failure was defined as HRF or LI and vasopressor use.

Student’s t test was utilized to compare continuous variables. Fisher’s Exact Test was used to compare dichotomous variables. Statistical significance was p < 0.05. Analysis was done using statistical software (SAS Proprietary Software Release 6.12; SAS Institute; Cary, NC).

RESULTS

Study Population

From March 1991 to April 1999, 1,301 patients received autologous PBSCT at UAMS. Seventy-eight patients (6%) received mechanical ventilation for ≥ 24 h. The mean age was 55.4 ± 12 years. Sixty-two percent were male patients. The indications for transplantation were multiple myeloma (n = 68; 87%), solid tumors (n = 7; 9%), and lymphoma (n = 3; 4%). The median duration of mechanical ventilation was 7 days (range, 1 to 63 days).

Hospital Survival and Mechanical Ventilation

Hospital survival for the autologous PBSCT patients was 20 of 78 patients (26%). Hospital survival for the multiple myeloma and nonmultiple myeloma autologous PBSCT patients was similar (18 of 68 patients [27%] and 2 of 10 patients [20%, respectively; p > 0.99). The two groups were combined for analysis. Table 1 shows the characteristics of hospital survivors and nonsurvivors for the autologous PBSCT patients. Median survival after extubation was 288 days (range, 35 days to 4 years). The 6-month and 1-year survival after extubation was 65% (13 of 20 patients) and 45% (9 of 20 patients), respectively. The date of death was available for 13 patients, and the cause of death was known in 7 patients: disease progression (multiple myeloma; n = 4), septic shock (n = 1), acute renal failure (n = 1), treatment-related toxicity (n = 1).

Survival and Organ Failure

Table 2 shows the influence of organ failure on hospital survival. The prevalence of no organ failure, isolated LI or isolated vasopressor use, and HRF was 27%, 51%, and 12%, respectively. Seventy-six percent (60 of 77 patients) of the autologous PBSCT patients receiving mechanical ventilation had no organ failure, isolated LI, or only required vasopresors. Hospital survival for patients with no organ failure, or had either isolated LI or only required vasopressors was 32% (19 of 60 patients), while

### Table 1—Characteristics of Hospital Survivors and Nonsurvivors Autologous PBSCT Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>20 (26)</td>
<td>55 (74)</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>55.9 ± 11.7</td>
<td>54.0 ± 11.7</td>
<td>0.54</td>
</tr>
<tr>
<td>Male sex</td>
<td>8 (40)</td>
<td>22 (38)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>18 (90)</td>
<td>50 (86)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td>0.57</td>
</tr>
<tr>
<td>Solid tumors†</td>
<td>2 (10)</td>
<td>5 (9)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>MV duration, d</td>
<td>11.5 ± 12.6</td>
<td>11.1 ± 11.9</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%) or mean ± SD. MV = mechanical ventilation.
†Breast cancer (n = 3), ovarian cancer (n = 2), testicular cancer (n = 1), and sarcoma (n = 1).
hospital survival for patients with HRF or LI and vasopressor use was 6% (1 of 17 patients). The 6-month survival for patients with no organ failure, or had isolated LI, or only required vasopressors was 20% (12 of 59 patients) vs 0% (0 of 17 patients) for patients who had LI and vasopressor use, and/or HRF.

Table 3 shows the 8-year study period divided into four 2-year periods. Hospital survival and the prevalence of organ system failures were described for each time period. Hospital survival improved over the study period. This improvement was due to improved survival in patients with no or one-organ system failure.

**DISCUSSION**

This study describes the survival for a large group of autologous PBSCT patients receiving mechanical ventilation. The principle finding of this study was that autologous PBSCT patients receiving mechanical ventilation without organ failure or with isolated LI or isolated vasopressor use represented 77% of all BSCT patients receiving mechanical ventilation, and those patients had better hospital survival (32%) than autologous PBSCT patients receiving mechanical ventilation with LI and vasopressor use and/or HRF (6%). The hospital survival for autologous PBSCT patients receiving mechanical ventilation with two-organ failure (HRF or LI and vasopressor use) was similar to the hospital survival reported in the medical literature for BMT patients receiving mechanical ventilation (4 to 13%).

In addition, the hospital survival for autologous PBSCT patients receiving mechanical ventilation improved over the 8-year study period (Table 3). This improvement was not due to a decrease in the prevalence of patients with two-organ failure. Similar improved survival over time was reported for BMT patients receiving mechanical ventilation. The apparent improvement in survival for BMT patients receiving mechanical ventilation over time may be due to changes in treatment(s), patient selection, and/or improvement in supportive care.

This is the first study to describe the survival for a large homogeneous group of autologous PBSCT patients receiving mechanical ventilation. In a study by Price et al., only 10 of 26 PBSCT patients receiving mechanical ventilation received an autologous PBSCT; the survival of the 10 autologous PBSCT patients was 30%, in line with our findings, in which the prevalence of mechanical ventilation after autologous PBSCT was 6%. Price et al. did not report the prevalence of mechanical ventilation for PBSCT patients. The prevalence of mechanical ventilation after BMT has varied from 16 to 29%. The current study found similar hospital survival for autologous PBSCT patients receiving mechanical ventilation with two-organ failure (HRF or LI and vasopressor use). None of the autologous PBSCT patients with HRF and only one patient with LI and vasopressor use survived to hospital discharge. None of the autologous PBSCT patients receiving mechanical ventilation with two-organ failure were

<table>
<thead>
<tr>
<th>Organ Failure</th>
<th>Patients</th>
<th>Hospital Survival</th>
<th>6-mo Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>No organ failure</td>
<td>21 (27)</td>
<td>8 (38)</td>
<td>5 (24)</td>
</tr>
<tr>
<td>LI or vasopressor use</td>
<td>39 (51)</td>
<td>11 (28)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Any two-organ failure†</td>
<td>17 (22)</td>
<td>1 (6)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%). Data are missing for one patient (nonsurvivor).
†LI and vasopressor use or HRF.

Table 3—Hospital Survival Over the 8-yr Study Period*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>7 (9)</td>
<td>13 (17)</td>
<td>25 (33)</td>
<td>32 (42)</td>
</tr>
<tr>
<td>Hospital survival</td>
<td>0 (0)</td>
<td>2 (15)</td>
<td>7 (27)</td>
<td>11 (35)</td>
</tr>
<tr>
<td>No or one-organ failure</td>
<td>7 (100)</td>
<td>11 (85)</td>
<td>18 (72)</td>
<td>24 (75)</td>
</tr>
<tr>
<td>Hospital survival</td>
<td>0 (0)</td>
<td>2 (18)</td>
<td>7 (39)</td>
<td>10 (42)</td>
</tr>
<tr>
<td>Two-organ failure†</td>
<td>0 (0)</td>
<td>2 (15)</td>
<td>7 (28)</td>
<td>8 (25)</td>
</tr>
<tr>
<td>Hospital survival</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (13)</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%).
†HRF or LI and vasopressor use.
alive at 6 months. In contrast, the hospital survival for autologous PBSCT patients receiving mechanical ventilation who did not have organ failure or who had isolated LI or only required vasopressors was 32%. Importantly, this group represented three fourths of all PBSCT patients receiving mechanical ventilation.

The reason why survival for autologous PBSCT receiving mechanical ventilation was better than BMT patients receiving mechanical ventilation is not known. Autologous PBSCT recipients, relative to BMT patients, generally receive less intense preparative regimens before transplantation, less immunosuppression after transplantation, and have faster marrow engraftment. A major cause of morbidity and mortality in allogenic BMT patients, graft vs host disease does not develop in autologous PBSCT patients. Presumably, rapid marrow engraftment with reconstitution of native immune function, less treatment-related organ toxicity, and the lack of graft vs host disease are important mitigating factors.

In this study, three fourths of autologous PBSCT patients did not have two-organ failure (HRF and/or LI and vasopressor use) after 72 h of mechanical ventilation, and their hospital survival was 32%. Physicians caring for these patients should be willing to provide mechanical ventilation. Subsequently, the patient’s clinical status must be closely monitored to determine if the response to treatment warrants continuing mechanical ventilation.

This study, which uses simple and readily available physiologic and laboratory data, is limited by its retrospective design. Risk stratification by organ system failure may address differences in patient severity of illness, but a validated severity of illness prediction model was not used to document equivalent physiologic derangement between patient groups.

CONCLUSION

Hospital survival for autologous PBSCT patients receiving mechanical ventilation who did not have two-organ failure was 32%, and prolonged mechanical ventilation is justified.

ACKNOWLEDGMENT: The authors thank Mr. Clyde Bailey from the Myeloma and Transplantation Research Center, Miss Angela Johnson from Medical Records, and Mr. Trey Spencer from the Department of Biostatistics.

REFERENCES
13 Quabeck K. The lung as a critical organ in marrow transplantation. Bone Marrow Transplant 1994; 14:S19–S28
14 Schuster DP. Everything that should be done—not everything that can be done. Am Rev Respir Dis 1992; 145:505–509