Lung Transplantation After Long-term Mechanical Ventilation*
Results and 1-Year Follow-up

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Background: Long-term mechanical ventilation is considered as a relative or absolute contraindication for lung transplantation by most centers. We report on the results of transplantation in nine patients requiring long-term mechanical ventilation at two lung transplant centers.

Methods: The study group (group 1) consisted of nine patients receiving mechanical ventilation who underwent lung transplantation at either Duke University Medical Center or the University of Florida between 1992 and 1997. Patients in group 1 met the following criteria: they underwent exercise therapy with a physical therapist, and they were without panresistant bacterial airway colonization. The study patients that met these criteria spent at least 13 days receiving mechanical ventilation prior to transplantation. The control population (group 2; n = 65) consisted of all patients who underwent transplantation at either center in the calendar year 1997 who were ventilator independent. The 1-year survival rates in each group were calculated by the Kaplan-Meier method. The number of days required for extubation in each group were compared by the nonparametric Wilcoxon rank sum test. The FEV₁ value at 1 year was reported in each group.

Results: The 1-year survival rates were 78% and 83% in group 1 and group 2, respectively. The mean number of days required until extubation were 41 days in group 1 and 9 days in group 2 (p < 0.01). The allograft function was comparable in the two groups at 1 year.

Conclusions: In a select population of ventilator-dependent patients, the 1-year survival rate is comparable to the standard lung transplant population. However, these ventilator-dependent patients require a significantly longer time until extubation than other transplant recipients.

Key words: lung transplantation; mechanical ventilation; survival rates

Abbreviations: BLT = bilateral lung transplantation; %IBW = ideal body weight; SLT = single lung transplantation

Lung transplantation has become an acceptable therapeutic option for patients with end-stage lung diseases. It has been successfully used in a wide variety of end-stage pulmonary parenchymal and vascular diseases. The success of transplantation is the result of following strict selection criteria, improved surgical techniques, and increasing experience with managing this patient population after transplantation.¹

Mechanical ventilation has been identified as a risk factor for early mortality after transplantation by the International Registry.² Thus, mechanical ventilation has been viewed as either an absolute or relative contraindication by most lung transplant centers, because airway colonization with bacteriamay lead to nosocomial infection and because respiratory muscle deconditioning may necessitate prolonged postoperative ventilatory support and prolonged recovery.³

This report describes the experience in two lung transplant centers with lung transplantation in patients requiring long-term mechanical ventilation. The outcome after transplantation in these patients was reviewed and compared to the patients who underwent transplantation and did not require mechanical ventilation prior to transplantation.

Materials and Methods

The study population (group 1) was limited to patients requiring mechanical ventilation prior to transplantation who met the following criteria: they were ambulatory, they underwent exercise therapy with a physical therapist, and they were colonized with sensitive bacteria. Nine patients who received mechanical ventilation for at least 13 days met these criteria. Seven patients who...
underwent transplantation and had received mechanical ventilation for < 12 days were excluded because they were all nonambulatory, and one patient receiving mechanical ventilation for 191 days was excluded because of the presence of panresistant *Pseudomonas aeruginosa* at the time of transplantation. All patients in group 1 underwent bronchoscopy at the time of intubation to assess for purulent secretions and to obtain bronchial washings for cultures. The selection criteria and the operative procedure of choice were identical for both the study and control patients, regardless whether they were ventilator dependent or not. Bilateral lung transplantation (BLT) was performed in patients with primary pulmonary hypertension or in patients with evidence of bilateral bronchiectasis by chest CT. All other patients underwent single lung transplantation (SLT). Active respiratory infection was diagnosed if there was temperature elevation (> 37.5°C) associated with a change in sputum quality or quantity, or a change in chest radiograph.

All patients in group 1 required mechanical ventilation 24 h/d prior to transplantation. Anticipating prolonged mechanical ventilation, tracheostomy was performed a few days after intubation to facilitate ambulation and pulmonary toilet. The cause of respiratory failure was respiratory acidosis secondary to progression of end-stage lung disease in seven of nine patients. Two of nine patients had acute bacterial pneumonia superimposed on end-stage lung disease as the cause of their respiratory failure. Eight of nine patients had at least one attempt at extubation prior to transplantation, but had ventilator failure (respiratory acidosis) after < 24 h, requiring reintubation of mechanical ventilation. Only one patient with a Pco₂ of 90 to 100 mm Hg on pressure-control mode of ventilation (with peak airway pressure of 40 cm H₂O) was maintained on mechanical ventilation without any attempts at extubation. Thus, the study group consisted of all ambulatory patients (colonized with sensitive bacteria) requiring at least 13 days of mechanical ventilation who underwent transplantation at either Duke University Medical Center or the University of Florida from 1992 to 1997. The first transplantation at Duke University took place in 1992, and at the University of Florida in 1994.

The control group (group 2) was defined as all patients who did not require mechanical ventilation prior to transplantation, and who underwent transplantation at either center in the calendar year 1997. The year 1997 was chosen for the control group because the majority of the study population in group 1 (six of nine patients) underwent transplantation in 1997. None of the patients in group 2 were colonized with panresistant bacteria. Sputum cultures in group 2 patients were obtained for patients with clinical or radiographic signs of bronchiectasis.

The results of a 6-min walk test, performed preoperatively, are reported for both groups of patients. The 6-min walk test was performed in group 1 with assisted ambulatory bag ventilation. The results of the 6-min walk test for the two groups were compared by the two tailed Student’s *t* test. The number of days required for extubation in each group were compared by the nonparametric Wilcoxon rank sum test. The 1-year survival rate in each group was calculated by the Kaplan-Meier method. The survival rates were then compared by the log-rank test. The mean allograft function between the two groups was compared by the unpaired Student’s *t* test. The mean number of readmissions (per patient) in the first 12 months were calculated and compared by the unpaired Student’s *t* test. A *p* value < 0.05 was considered statistically significant.

## Results

There were nine patients in group 1, of whom four patients underwent SLT and five patients underwent BLT (Table 1). There were 65 patients in group 2, of whom 44 patients underwent SLT and 21 patients underwent BLT (Table 1). Five of nine patients in group 1 were colonized with *P. aeruginosa* (each patient had sensitivity to at least one antibacterial agent) prior to transplantation. All patients in group 1 were ambulatory while receiving mechanical ventilation, and were actively participating in a pulmonary rehabilitation program. Six of nine patients in group 1 were awaiting lung transplantation in the hospital, while the rest were awaiting lung transplantation at home. The ideal body weight (%IBW) and the 6-min walk test, performed preoperatively, of patients in group 1 are reported (Table 2).

The 6-min walk test was performed preoperatively by 7 patients in group 1 and 52 patients in group 2. The mean results in group 1 and group 2 were 475 feet and 771 feet, respectively. The difference was not statistically significant (*p* = 0.09). The mean number of days receiving ventilation prior to transplantation in group 1 was 369 days (median, 162 days; range, 13 to 2,160 days). The mean number of days required until extubation after lung transplantation in group 1 was 41 days (median, 16 days), compared to a mean of 9 days in group 2 (median, 1 day; *p* < 0.01; Table 2). Seven patients (three SLTs and 4 BLTs) in group 1 survived at least 1 year after transplantation. The 1-year survival rates of group 1 and group 2 were 78% and 83%, respectively (*p* > 0.05; Fig 1).

In group 1, one BLT recipient died in the first 24 h secondary to bacterial sepsis, and one SLT recipient died at 5 months secondary to post-transplant lymphoproliferative disease.

The allograft function (FEV₁) at 12 months is reported in group 1 (Table 2). One patient in group 1 (patient 7) who underwent BLT had a suboptimal allograft function at 1 year after transplantation due to primary allograft failure. Another patient in group 1 with Williams-Campbell syndrome (patient 8), who also had BLT, had suboptimal allograft function 1

<table>
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<tr>
<th>Indications</th>
<th>Group 1</th>
<th>Group 2</th>
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<tr>
<td></td>
<td>SLT</td>
<td>BLT</td>
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<tr>
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<tr>
<td>Bronchiectasis</td>
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<tr>
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*IPF = idiopathic pulmonary fibrosis; PPH = primary pulmonary hypertension; ES = Eisenmenger’s syndrome.
†This patient underwent concomitant right coronary artery bypass surgery.

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year after transplantation secondary to bronchiectasis from recurrent bacterial infections. Autopsy at 18 months after transplantation showed severe bilateral bronchiectasis without any evidence of obliterative bronchiolitis. The FEV₁ at 1 year was thus calculated in a subset of patients in group 1 (five patients). Five patients in group 1 who survived to at least 1 year after transplantation had allograft function comparable to group 2. The mean FEV₁ for SLT was 47% (n = 3), and the mean FEV₁ was 82% for BLT (n = 2, excluding patient 7 and patient 8) at 12 months after transplantation in group 1 patients. There was no evidence of bronchiolitis obliterans syndrome in group 1 patients at 1 year after transplantation, both by physiologic and pathologic criteria. The mean FEV₁ was 51% and 78% (of predicted) for SLT and BLT, respectively, at 12 months after transplantation in group 2 patients.

All patients in group 1 were able to perform activities of daily living without assistance at 3 months after transplantation and throughout the remainder of the 12 months of follow-up. All patients in group 1 were independent of oxygen at 3 months after transplantation, except for one patient (patient 7) who required supplemental oxygen to be able to perform activities of daily living after transplantation. The rates of readmission in the first 12 months after transplant surgery were similar between patients in group 1 and group 2 (1.6 and 1.3 readmissions, respectively; p > 0.05).

**Discussion**

Ventilator dependency is considered as a relative or absolute contraindication to lung transplantation by most centers. These patients have been historically excluded because of concerns regarding airway colonization and the possible risk of posttransplant pneumonia. Moreover, long-term immobility and bed rest associated with mechanical ventilation predisposes this population to severe deconditioning and delays recovery after transplantation. Approximately 3% of lung transplant recipients in the United States have been ventilator dependent at the time of surgery. There is a three-fold increase in the 1-year mortality in these patients compared to the recipients who did not receive ventilation.

![Figure 1. Comparison of 1-year survival rates between group 1 and group 2.](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21956/)
We report on a select population of recipients who have been ventilator dependent for at least 13 days prior to lung transplantation. Seven of nine of our patients were already on the lung transplant waiting list and had accrued time prior to their respiratory failure. All ventilator-dependent patients in this report underwent active exercise therapy with a physical therapist, all were colonized with bacteria sensitive to at least one antibacterial agent, and all weighed in the 70 to 130 percentile of their %IBW. Moreover, none of our group 1 patients required > 60% fraction of inspired oxygen and none had peak airway pressures > 40 cm H2O prior to transplantation.

This series includes patients who had been receiving mechanical ventilation for periods of up to 6 years, without any hope for extubation short of lung transplantation. This select population of ventilator-dependent patients had a 1-year survival rate comparable to the patients who did not receive ventilation and who underwent transplantation at the two centers during the same period of time. However, patients requiring mechanical ventilation prior to transplantation spent a significantly longer time receiving ventilation after transplantation compared to our control group. It is tempting to attribute the longer posttransplant ventilation in group 1 to musculoskeletal deconditioning; but we found no correlation between the 6-min walk test or the number of days receiving ventilation prior to transplant, and the number of days required until extubation after transplantation. Moreover, there was no correlation between the 6-min walk test (performed prior to transplantation) and the mortality after transplantation. It is conceivable that a more comprehensive test (such as complete cardiopulmonary exercise testing) may have amplified the difference in the respiratory muscle conditioning between the groups.

The allograft function in the two groups (excluding patients 7 and 8 in group 1) was comparable at 12 months after transplantation. Patients in group 1 had a comparable functional result after transplantation compared to patients in group 2, in that they were all independent and were able to perform activities of daily living without help. All patients in group 1 (except patient 7) were independent of oxygen in the first 12 months after transplantation. Patients in group 1 and group 2 also had a similar rates of re-admission to the hospital in the first 12 months after transplantation.

The 1-year survival rates of our report must be interpreted with caution, as our ventilator-dependent patients are a select population, with a relatively small sample size. Thus, it is possible that the 1-year survival may prove to be statistically significant with a larger group 1 sample size. However, the outcome of the ventilator-dependent transplant recipients in our report differs from the national lung transplant registry results. This is most likely because our population is a select population of medically stable patients maintained chronically with mechanical ventilation, in contrast to the national registry, which probably includes ventilator-dependent recipients who are more critically or acutely ill at the time of transplantation. Our report also differs from the previously reported cases of ventilator-dependent patients, in that it specifically included recipients who were receiving ventilation for at least 13 days prior to transplantation, and also in that we reported on the survival rate and allograft function at 1 year after transplantation. The published literature discusses a total of 20 cases of ventilator-dependent patients, 15 of whom required < 2 weeks of mechanical ventilation prior to transplantation, and with the longest patient requiring 4 months of ventilator support prior to transplantation.

In conclusion, patients who are thoroughly evaluated for transplantation, who remain ambulatory, and who are without major medical complications or end-organ dysfunction should be considered for lung transplantation even if they are ventilator dependent for long periods. Carefully selected patients receiving long-term mechanical ventilation do not seem to be at excessive risk of mortality in the first year after transplantation. However, they will spend significantly more time receiving mechanical ventilation after lung transplantation than standard transplant recipients.

REFERENCES
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