Outcomes of Children With Severe Bronchopulmonary Dysplasia Who Were Ventilator Dependent at Home

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**Key Words:** Bronchopulmonary dysplasia, outcome, positive pressure ventilation, tracheostomy, home

**Abbreviations:**
- BPD—bronchopulmonary dysplasia
- HVP—home ventilator program
- IQR—interquartile range
- IVH—intraventricular hemorrhage
- PPV—positive pressure ventilation

Dr Cristea conceptualized and designed the study, collected the data, and drafted the initial manuscript; Dr Carroll carried out the initial analyses and reviewed and revised the manuscript; Dr Davis provided guidance with study design and critically reviewed the manuscript; Dr Swigonski facilitated communication with Indiana State Department of Health and critically reviewed the manuscript; Dr Ackerman provided guidance with study design and data collection and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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**Objective:** To describe the incidence and outcomes of children with chronic respiratory failure secondary to severe bronchopulmonary dysplasia (BPD) on chronic positive pressure ventilation (PPV) via tracheostomy at home.

**Methods:** We retrospectively reviewed medical charts of patients with severe BPD who were PPV dependent at home and who were enrolled in a university-affiliated home ventilator program between 1984 and 2010. We excluded patients with other comorbidities that could contribute to the development of chronic respiratory failure. We reported the incidence of these children in Indiana and cumulative incidences of survival, liberation from PPV, and decannulation.

**Results:** Over 27 years, 628 children were cared for in our home ventilator program. Of these, 102 patients met inclusion criteria: 83 (81.4%) were alive and 19 (18.6%) were deceased. Sixty-nine patients (67.6%) were liberated from PPV, and 97.1% of them were weaned before their fifth birthday, with a median age at liberation of 24 months (interquartile range, 19–33). Similarly, 60 patients (58.8%) were decannulated, of which 96.7% completed this process before their sixth birthday, with a median age at decannulation of 37.5 months (interquartile range, 31.5–45). The incidence of children with chronic respiratory failure secondary to BPD who were PPV-dependent at home in Indiana was 1.23 per 100 000 live births in 1984 and increased to 4.77 per 100 000 live births in 2010.

**Conclusions:** Although extreme prematurity associated with severe BPD necessitating PPV at home carries significant risks of morbidity and mortality, successful liberation from mechanical ventilation and decannulation are likely to occur. PEDIATRICS 2013;132:e727–e734
First characterized by Northway and colleagues in 1967, bronchopulmonary dysplasia (BPD) is a known complication of prematurity, defined as the presence of persistent signs and symptoms of respiratory distress, tachypnea, hypoxemia necessitating supplemental oxygen, and an abnormal chest radiograph at 36 weeks’ postmenstrual age. In recent years, advancements made in the prevention of BPD, such as prenatal glucocorticoids, surfactant use, and lung protective ventilation strategies, have led to changes in the pathologic findings and clinical course of this condition. The “new” BPD is a manifestation of lung immaturity characterized by inflammation, dysmorphic alveolar and vascular structures, and a decreased surface area for gas exchange.

The incidence and prevalence of patients with severe BPD necessitating positive pressure ventilation (PPV) at home are unknown. The first estimates of ventilator-dependent children (<21 years of age) in the United States were published in the 1980s, with an estimated prevalence of 0.7 to 2 per 100,000 children; current state-level estimates show an increasing prevalence of home-ventilated children. For instance, in Utah the prevalence of these children has increased from 5.0 per 100,000 in 1996 to 6.3 per 100,000 in 2004. The 2005 Massachusetts census of children on chronic mechanical respiratory support shows a nearly threefold increase in this population in the 15-year interval since the last census. In addition, the rate of hospital discharges for all children dependent on long-term mechanical ventilation increased 55% from 2000 to 2006.

The respiratory outcomes of patients with BPD range from no oxygen requirement to chronic ventilator dependence. Various publications address the outcome of the least severe types of BPD, yet very limited data exist on BPD-related chronic respiratory failure. Given the limited published outcome data for children with severe BPD, we sought to define the long-term respiratory morbidity of this condition by evaluating the incidence and outcomes of patients with severe BPD who needed chronic PPV via tracheostomy at initial discharge from the hospital.

**METHODS**

We conducted a retrospective cohort study of all patients diagnosed with BPD who needed full-time PPV via tracheostomy at home. These patients were followed in the Pediatric Pulmonology Clinic Home Ventilator Program (HVP) at Riley Hospital for Children, Indiana University, Indianapolis. This clinic was founded in 1984 and is the only comprehensive clinic of this type in the state, where children and young adults who need respiratory support at home are followed on a regular basis. The medical care has been very consistent, provided by the same pulmonary and critical care physician (V.A.), a dedicated nurse with special pulmonary expertise, respiratory therapists, and a social worker. The HVP team was usually involved in these patients’ care before their discharge from the hospital. If the PPV was initiated during childhood, that patient is followed in the HVP clinic, regardless of age. Although it follows general principles, the ventilator weaning protocol used in this clinic is individualized to each patient. Weaning candidates are those who are stable at home and thriving. The ventilator settings are slowly weaned over several months. Weight gain and indirect carbon dioxide levels (obtained via basic metabolic panels) are monitored. When low respiratory support is achieved during the day, short-off ventilator trials are initiated. In the months that follow, the time off ventilator while awake is gradually increased. The patient’s status off ventilator support while asleep is assessed through an overnight polysomnogram.

If there is no significant hypercarbia, severe desaturation, or tachypnea, night ventilator support is discontinued. The patient is seen monthly during weaning. Most patients receive 8 to 12 hours of skilled nursing per day. Respite care is available through specialized pediatric facilities but not routinely provided through the HVP. During the study period the most common ventilator used at home was the LP series (Covidien, Mansfield, MA), with transition to the LTV (Pulmonetic Systems, Inc., Minneapolis, MN) when this type of ventilator became available.

Patients with associated comorbidities that could contribute to the development of chronic respiratory failure were excluded from this study; these comorbidities include history of chest surgery and chromosomal, anatomic, metabolic, and neurologic abnormalities. We also excluded patients with BPD who received a tracheostomy and became PPV dependent in a subsequent hospital admission to eliminate other acute causative factors. Our study was approved by the Indiana University School of Medicine Institutional Review Board.

The first author (A.I.C.) reviewed all medical records for each patient, including the hospital’s electronic records, the Pediatric Pulmonology Clinic Home Ventilator Program charts, and the HVP paper charts. Data elements abstracted were gestational age, birth weight, gender, race, health insurance, date when the patient became technology independent, and date of decannulation.
[diagnosed by echocardiography], systemic hypertension, necrotizing enterocolitis, patent ductus arteriosus), date of discharge, and destination after discharge (home, foster home, chronic care facility). All subsequent readmissions were recorded, along with the main diagnosis at discharge from the hospital. Survival status was defined as alive or deceased. Final respiratory status was defined as PPV dependent, weaned off PPV, or decannulated. Data are presented as proportions or as medians and interquartile ranges (IQRs). Descriptive characteristics were compared by using Fisher’s exact tests for categorical variables and Mann–Whitney–Wilcoxon rank sum test for continuous variables.

The incidence of children with severe BPD who were PPV dependent at home was calculated by dividing the number of patients born in one year into the total number of children born in that particular year, as reported by Indiana State Department of Health vital statistics birth data.16

We constructed Kaplan–Meier survival curves and cumulative incidence curves for liberation from PPV and decannulation. Cox proportional hazards models17 were performed for the outcomes death, liberation from PPV, and decannulation, using the following covariates: birth weight (≤750 g or >750 g), gender, race, and severe IVH. Gestational age was not used in this analysis because of its very high correlation to birth weight. Statistical significance was determined with a P value of .05. Data were analyzed by using SAS software (version 9.3; SAS Institute, Inc, Cary, NC).

RESULTS

Between 1984 and 2010, 628 children receiving part- or full-time PPV via tracheostomy were cared for in the HVP. As of December 2010, 207 patients followed in this clinic were diagnosed with BPD. One hundred five (50.7%) of these patients were excluded based on the exclusion criteria noted in the Methods section. Of these, 72 patients had chest surgery (secondary to tracheoesophageal fistula, congenital diaphragmatic hernia, or congenital cardiac disease), 8 patients had neurologic abnormalities (Chiari malformation, myelomeningocele), 7 patients had chromosomal abnormalities (trisomy 21, 18, 13), 4 patients had lung or chest anatomic abnormalities (lobar emphysema, hypoplastic lung, thoracic insufficiency syndrome), 3 patients had metabolic disease, 3 patients became ventilator dependent after viral infection acquired after initial discharge from the hospital, 2 patients had congenital cytomegalovirus infection, and 2 patients had fetal alcohol syndrome. Four patients were not followed anymore at our institution: 3 moved out of state at a very young age, when they were still PPV dependent, and 1 patient was liberated from ventilation but still tracheostomy dependent.

One hundred two (49.3%) patients who carried the diagnosis of severe BPD and were receiving full-time PPV via tracheostomy at initial hospital discharge were included in this study. These patients were intubated at birth or soon after because of prematurity and respiratory distress syndrome. The only documented indication for tracheostomy in this cohort was chronic respiratory failure necessitating mechanical ventilation. These patients were followed for a total of 871 person-years. The characteristics of subjects grouped by their survival status are shown in Table 1. Eighty-three (81.4%) of 102 patients were alive and 19 (18.6%) were deceased. There were no significant differences between the alive and deceased groups, in any demographic characteristics.

The incidence of children with chronic respiratory failure secondary to BPD who were PPV dependent at home in Indiana was 1.23 per 100 000 live births in 1984 and increased to 4.77 per 100 000 live births in 2010.

Morbidity during the initial neonatal intensive care unit hospitalization included the following: 102 (100%) patients received a gastrostomy tube (33.3% also had a Nissen fundoplication), 45 (44.1%) patients were diagnosed with retinopathy of prematurity, 26 (25.5%) patients had severe IVH that necessitated ventriculoperitoneal shunt, 14 (13.7%) patients had seizures, 28 (27.4%) patients had documented sepsis, 22 (21.5%) patients had inguinal hernia repair, 20 (19.6%) patients had pulmonary hypertension, 16 (15.6%) patients had systemic hypertension, 13 (12.7%) patients were diagnosed with necrotizing enterocolitis, and 19 (18.6%) patients had patent ductus arteriosus, of which 11 needed surgical ligation.

The rehospitalization rate for this cohort was impressive, with a total number of 675 events. The incidence of rehospitalization was significantly higher before decannulation (554 vs 121 events, P < .0001). The most common reason for rehospitalization was respiratory related (558 before decannulation versus 87 after decannulation, P < .0001), followed by a need for surgical interventions (54 before decannulation versus 16 after decannulation, P = .36).

Figure 1 illustrates the Kaplan–Meier survival curve for 102 patients with severe BPD who were discharged on home PPV, along with the survival incidence stratified by birth weight (≤750 g or <750 g). Figure 2 represents the Kaplan–Meier curve showing the cumulative proportion of live patients liberated from PPV and decannulated. Within the group of patients who were alive at the end of this study, 69 (83.1%) patients were weaned off the PPV and 60 (72.2%) patients were decannulated. Sixty-seven (97.1%) of 69 patients liberated from PPV were
weaned within the first 5 years of life, with a median age at liberation of 24 months (IQR, 19–33). Similarly, 58 (96.7%) of the 60 decannulated patients completed this process within the first 6 years of life, with a median age at decannulation of 37.5 months (IQR, 31.5–45). The median interval between liberation from PPV and decannulation was 11 months (IQR, 7–16).

At the end of the study period, 14 patients were still PPV dependent. Ten patients were 29 months of age or younger, with a median of 13.5 months (IQR, 9.75–25). These patients were expected to follow a similar path of liberation from ventilation and decannulation. Four patients were 16 years of age or older. While liberated from PPV, 9 patients were still tracheostomy dependent. Their median age was 22 months (IQR, 19.5–84).

Within the group of deceased patients, 10 (52.6%) patients died while on PPV, and 5 (26.3%) others were tracheostomy collar dependent. The median age at death was 27 months (IQR, 16–60). The circumstances of death were not known for the majority of these patients, because most of them died at home, and no autopsies were performed. For those who had a documented

### TABLE 1 Baseline Characteristics of 102 Children With Severe BPD Who Were PPV Dependent via Tracheostomy at Home

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Alive, N = 83 (%)</th>
<th>Deceased, N = 19 (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>50 (60)</td>
<td>14 (74)</td>
<td>.30</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>57 (69)</td>
<td>13 (68)</td>
<td>.83</td>
</tr>
<tr>
<td>African American</td>
<td>20 (24)</td>
<td>4 (21)</td>
<td></td>
</tr>
<tr>
<td>Other (Hispanic, Asian)</td>
<td>6 (7)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td>Birth wt (g)*</td>
<td>762.5* (650–974)</td>
<td>700* (560–770)</td>
<td>.07</td>
</tr>
<tr>
<td>Gestational age (wk)*</td>
<td>26 (25–27)</td>
<td>26 (25–27)</td>
<td>.84</td>
</tr>
<tr>
<td>Health insurance, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>50 (61)</td>
<td>11 (58)</td>
<td>.72</td>
</tr>
<tr>
<td>Private and Medicaid</td>
<td>14 (17)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>18 (22)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td>Initial hospital stay</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length (mo)*</td>
<td>10* (8–12)</td>
<td>10.5* (8.5–12)</td>
<td>.94</td>
</tr>
<tr>
<td>Discharge destination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>65 (78)</td>
<td>14 (74)</td>
<td>.26</td>
</tr>
<tr>
<td>Foster home</td>
<td>11 (13)</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>Chronic care facility</td>
<td>7 (8)</td>
<td>4 (21)</td>
<td></td>
</tr>
</tbody>
</table>
| a Results reported as median (interquartile range).  
| b Birth wt was missing for 6 patients.  
| c Birth wt was missing for 2 patients.  
| d Date of discharge was missing for 6 patients.  
| e Date of discharge was missing for 3 patients. 

**FIGURE 1**

Kaplan–Meier survival curve for 102 patients with severe BPD who were PPV dependent at home.
cause of death in their medical records, 2 deaths were tracheostomy related (accidental decannulation), 2 deaths were expected (because the patients had “do not resuscitate” orders), and 2 other deaths were secondary to cardiorespiratory arrest. There was no documentation of death caused by ventilator malfunction for any of these patients.

Table 2 provides the hazard ratios and the 95% confidence intervals for the Cox proportional hazards analyses. Patients with a lower birth weight had greater odds of an earlier death.

DISCUSSION
This study of 102 children with respiratory failure secondary to severe BPD who were discharged from the hospital on PPV represents the largest cohort of such children with the longest follow-up reported to date. More than 80% of children survive, and most of them were liberated from PPV and decannulated. Our data suggest that if a child is not off PPV by 5 years and decannulated by 6 years, he or she is unlikely to become so (in our study, only 2 [2.4%] patients were weaned beyond that time period). This information is important for families and for health care providers for planning long-term health needs.

In general, children on home mechanical ventilation are a heterogeneous population with varied indications for chronic ventilation and severity of comorbidities. Earlier studies included a range of subgroups of patients, follow-up periods, geographic sites, and different periods with diverse technology. Because of these differences, it is difficult to compare patients’ outcomes across studies. The incidence of mortality reported in other studies from different time periods, where patients’ outcomes are reported by the original cause of respiratory failure, was higher than or similar to our results. The incidence and the timing of liberation from home mechanical ventilation are consistent with those in another study with similar follow-up periods. The question of the racial or ethnic and gender disparity in mortality among premature infants with BPD remains open to interpretation, with studies reporting conflicting results. Our regression analyses showed that race, gender, and IVH necessitating shunt was not associated with death. Other races (Asians and Hispanics) were less likely than Caucasians to be liberated from PPV or decannulated, but it is difficult to speculate on the causal relationship, which may include cultural and religious factors that influence

FIGURE 2
Cumulative incidence of liberation from PPV and decannulation for 83 alive children with severe BPD.
TABLE 2 Cox Proportional Hazards Model of Death, Liberation From PPV and Decannulation, Controlling for Gender, Race, Birth Wt, and IVH

<table>
<thead>
<tr>
<th>Variable</th>
<th>Death</th>
<th>Liberation From PPV</th>
<th>Decannulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female versus male</td>
<td>0.41 (0.13, 1.50)</td>
<td>0.72 (0.25, 2.03)</td>
<td>0.82 (0.37, 1.79)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American versus Caucasian</td>
<td>0.76 (0.21, 2.79)</td>
<td>1.11 (0.30, 4.10)</td>
<td>1.14 (0.44, 2.99)</td>
</tr>
<tr>
<td>Other versus Caucasian</td>
<td>3.35 (0.68, 16.59)</td>
<td>7.54 (2.36, 24.12)</td>
<td>5.51 (2.05, 14.83)</td>
</tr>
<tr>
<td>Birth wt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤750 g vs &gt;750 g</td>
<td>0.34 (0.12, 0.99)</td>
<td>1.20 (0.46, 3.13)</td>
<td>0.55 (0.26, 1.17)</td>
</tr>
<tr>
<td>IVH</td>
<td>0.97 (0.33, 2.82)</td>
<td>1.33 (0.47, 3.78)</td>
<td>1.00 (0.47, 2.13)</td>
</tr>
</tbody>
</table>

* Results reported as hazard ratio (95% confidence interval).

health care decisions. We also showed that lower weight was associated with earlier death, a finding supported by earlier studies.29–31

Although several articles32,33 report a higher readmission rate in the first year of life for patients with BPD in general, we could not report the readmission rate for the first year of life because the length of the initial hospital stay was very long. This length of stay is probably secondary to the need for extensive caregiver training in ventilator and tracheostomy care, as previously described.34

We reported the number of hospitalizations before and after decannulation. The rehospitalization rate was significantly higher before decannulation; the most frequent reason for rehospitalization was respiratory related, as previously described.35,36 Although no other studies have addressed the rehospitalization rates for children with tracheostomy, before and after decannulation, several have found that children who are ventilator dependent at home have a higher risk of rehospitalization than other children.11,12,36–39

The decrease in readmission rate after decannulation may be secondary to removal of the tracheostomy, improvement in BPD, or both.

Major practice changes occurred during the 27 years of the study.5–6 We did secondary analyses (data not shown) to test whether practice changes were associated with changes in our outcomes. Our data showed that more patients with severe BPD who needed prolonged PPV at home were born after 1996, when prenatal corticosteroids and surfactant became widely used. Statistical comparisons were made between the groups of patients born before or during versus after 1996. There were no significant differences between these subgroups of patients, with the exception of the length of the initial hospital stay, which was shorter for those born after 1996 (P = .01). These findings are probably secondary to the major changes in the management of premature babies, which led to the improved survival of smaller, less mature infants in the 1990s.29

Our study has several limitations. First, this is a retrospective chart review, and we focus on the diagnosis of severe BPD as the only cause of respiratory failure in these patients. Second, we were unable to evaluate neurocognitive outcomes. Third, we could not identify the cause of death for several of the deceased patients. Fourth, during the study period only a few types of home ventilators were used, to ensure consistency in care provided by respiratory care practitioners both at home and in the hospital setting. We cannot comment on other types of ventilators available for use at home. Furthermore, we are reporting one institution’s experience and recognize that common practices may be different at other centers. The methods described here should not be considered the standard but rather one starting point for evaluation and improvement of the quality of care for these patients. Finally, our incidence data may be underestimated because they are based on our group of patients and state birth rate, possibly ignoring children who live closer to the state borders and receiving care in neighboring states.

The decision to take a baby home from the hospital with significant technological support comes with significant emotional burden for families. Our study provides new outcome data to support parents’ and medical teams’ decisions in caring for premature infants with severe BPD who need ventilatory support at home. Multi-institutional outcome research with better stratification of factors that can influence mortality and successful weaning protocols from PPV and decannulation are needed. Home ventilator programs should provide quality assurance and frequent monitoring not only for survival but for liberation from ventilation and decannulation to optimize care, minimize health care costs, and ensure that the clinical outcomes are comparable with those of other institutions.

CONCLUSIONS

Extreme prematurity associated with severe BPD necessitating PPV at home carries significant risks of morbidity and mortality. However, successful liberation from PPV and decannulation is likely to occur. Before this study, there were no long-term outcome data on the mortality and morbidity associated with home ventilation of children with severe BPD. This study offers valuable information that will enable health care providers and families to better plan for the medical care of these vulnerable infants. Prospective multicenter studies are necessary to elucidate the trends in outcomes of children with severe BPD and to standardize the care provided to these children.
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