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Retrospective Analysis of an Interdisciplinary Ventilator Care Program Intervention on Survival of Infants with Ventilator-Dependent Bronchopulmonary Dysplasia

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Abstract

Background—The clinical needs of infants with severe bronchopulmonary dysplasia (BPD) that remain ventilator-dependent are complex, and management strategies that optimize survival and long-term outcomes controversial. We hypothesized that an interdisciplinary ventilator care program (VCP), committed to the care of this population will improve survival through standardized approaches to cardiopulmonary care and related comorbidities, enhanced communication, and continuity of care.

Methods—Retrospective chart reviews were performed on patients at Children's Hospital Colorado's neonatal intensive care unit, who underwent tracheostomy placement between 2000 and 2013. Data were collected for two time periods: 2000 to 2005 and 2006 to 2013, before and after initiation of the VCP. Collected data on infants with ventilator-dependent BPD included: gestational age (GA), age at tracheostomy, respiratory severity score (RSS; mean airway pressure [MAP] $\times$ fraction of inspired oxygen [FiO₂]), comorbidities, medication use, and the age of death. Tracheostomy patients without severe BPD were excluded.

Results—Despite no difference, pre and post VCP regarding GA, birth weight or morbidities and survival to discharge increased from 50% to 85% after implementation of the VCP ($p < 0.05$). Between period 1 and 2, there were differences in systemic and inhaled steroid use and mucolytic use.

Conclusion—These findings suggest an interdisciplinary approach to the care of infants with ventilator-dependent BPD can improve survival.

Keywords

bronchopulmonary dysplasia; tracheostomy; ventilator-dependent; ventilator care program; interdisciplinary care

Bronchopulmonary dysplasia (BPD) is the chronic lung disease of infancy that occurs after premature birth.¹ Therapeutic advances such as antenatal steroids, postnatal surfactant, and improved ventilator strategies have led to improved survival at lower gestational age (GA), however, the prevalence of BPD has not declined.^{2–4} In 2001, Jobe et al, as part of a NIH consensus statement, defined BPD on a scale of mild, moderate, and severe, based on the need for supplemental oxygen and degree of respiratory support at 36 weeks corrected gestation or the time of discharge.⁵ While this statement provided more standardized assessments of BPD, it did not encompass the wide range of disease severity within the group classified as “severe BPD,” with some patients in this group ventilator-dependent beyond term-corrected GA. The incidence of ventilator-dependent BPD has been reported as 0.5 to 2% in infants weighing less than 1,500 g at birth.^{6–8} In infants whose birth weight is less than 1,000 g, the incidence may be as high as 6.9%.⁸ Mortality for this subset of patients remains high, ranging from 15 to 44%.^{7,9–14} Due to the low incidence of ventilator-dependent BPD at any single center, this population is understudied with many gaps in knowledge and controversies regarding optimal strategies to improve outcomes.

In addition to comorbidities that contribute to adverse outcomes in ventilator-dependent BPD, we speculate that there are several other factors that contribute to increased morbidity and mortality in this population. First, there are few evidence-based strategies that have been proven as effective in this population. Second, patients with chronic ventilator-dependent BPD have historically been cared for in acute care settings, in which infants with severe acute illness often necessitate precedence over chronic patients. Management strategies for chronic disease differ considerably from acute to chronic disease, especially regarding approaches to mechanical ventilation.¹⁵ When compared with approaches toward acute respiratory failure, neonatal intensive care unit (NICU) and pediatric intensive care unit providers may have less experience with the complexities of ventilator management of infants with severe chronic lung disease.

Perhaps most importantly, poor communication between providers, subspecialists, nursing staff, and families during prolonged hospitalizations may lead to inconsistent care and adverse outcomes in this population. Several factors, such as high staff turnover and infrequent communication among the doctors and bedside staff as well as between parents and the medical team may contribute to these inconsistencies. In addition, these infants have complex clinical courses with multiple morbidities, and are frequently hospitalized for more than a year,^{7,8} resulting in poor continuity of care. For these reasons, interdisciplinary care teams have the potential to alleviate many of these issues and improve outcomes for these infants.

In 2003, the American Thoracic Society published a consensus statement pertaining to the care of children with BPD.¹⁶ This report emphasized the need for an interdisciplinary approach to address the multi-organ sequelae of premature birth. More specifically, infants

with severe ventilator-dependent BPD are at increased risk for adverse neurodevelopmental outcomes, pulmonary hypertension (PH), gastroesophageal reflux (GER), feeding difficulty, airways disease, retinopathy of prematurity (ROP), and systemic hypertension.¹⁷ These comorbidities frequently complicate the course in BPD, require the involvement of multiple subspecialists, and when not integrated into the overall management plan, can further exacerbate gaps in communication and care. In centers that have adopted this approach to care, survival for this subset of infants is 75 to 80%,^{7,8} supporting an interdisciplinary, programmatic approach.

To address these issues, we developed a ventilator care program (VCP) to standardize approaches to the multisystem morbidities associated with severe ventilator-dependent BPD, to improve communication and continuity of care, and ultimately to improve survival.

Methods

With institutional review board approval, we performed retrospective chart reviews on all patients in our NICU who underwent tracheostomy placement for severe BPD. Patients were identified using a pre-existing neonatal database. Patients undergoing tracheostomy for reasons other than severe BPD were excluded from analysis.

Ventilator Care Program Management Strategies

Data were collected for two periods: 2000 to 2005 (prior to establishment of the VCP) and 2006 to 2013 (after the VCP was formed). The VCP team is an inpatient team that consists of medical specialists (neonatology, pulmonology, otolaryngology, pediatric surgery), respiratory therapists, nurses, pediatric and neonatal nurse practitioners, developmental specialists, therapists (occupational, physical, speech), and dietitians. Case managers, social workers, and chaplains also contribute to the care of many patients (Fig. 1).

To improve communication, the VCP began weekly interdisciplinary bedside rounds, with the primary NICU service, the VCP team, the bedside nurse, and the child's family. These rounds provide the opportunity for nurses, therapists, and families to express all of their concerns and the primary team and subspecialists to formulate a collaborative plan.

In addition to this approach utilizing team management, several changes in clinical care were adopted over time (Table 1) to address the most common contributors to mortality in our institution. These changes addressed the underlying physiology of respiratory insufficiency in BPD as well as common contributors to mortality in these patients at our institution (PH, GER and aspiration, tracheobronchomalacia, and withdrawal of support when care is deemed futile).

More specifically, with respect to ventilator strategies, we adopted an individualized approach geared toward addressing the multifactorial contributors to respiratory failure specific to each patient (heterogeneous lung disease with areas of hyperinflation alternating with areas of atelectasis,^{8,18} inflammation, large [tracheobronchomalacia,^{19,20}] and small airways obstruction and reactivity,^{21,22} excessive mucus production, and plugging⁸), screening, early detection and a coordinated treatment approach to PH, and prevention of

reflux and aspiration with fundoplication and gastrostomy tube placement for all infants (Table 2).

Patients are initially stabilized on volume-guarantee mechanical ventilators, with settings aimed at providing the support necessary to manage chronic respiratory distress, air hunger, and dyspnea with less emphasis on improving gas exchange. Such strategies include tracheostomy placement for chronic ventilation, establishing the patient-specific factors contributing to chronic respiratory insufficiency, and utilizing ventilator settings geared toward managing each child's underlying physiology.¹⁵ This goal is achieved by phenotyping patients utilizing high-resolution computerized tomography scanning to define the heterogeneity of the parenchymal lung disease, flexible bronchoscopy to screen for large airways malacia, and trials of bronchodilator therapy to determine airways reactivity. Excessive mucus production and secretions, superimposed upon a weak cough, as well as inline suctioning without saline (dry), results in poor mucus clearance and airways obstruction secondary to mucus plugging. It is our anecdotal experience that this is an often under-recognized contributor to chronic respiratory insufficiency and determining the contribution of secretions to respiratory failure and optimizing mucus clearance is essential to optimizing management. Ventilator strategies geared toward management of this complex physiology differ considerably from the "lung protective" strategies of acute respiratory failure (Table 2).¹⁵

Since PH is a major contributor to mortality in these infants,^{9–11} all infants were screened for PH by echocardiogram at least at 36 weeks' GA. This differed considerably from our approach during period 1, where patients were not screened for PH, and the diagnosis of PH made when patients were symptomatic (having episodes of desaturation, after instability with induction of anesthesia, high fraction of inspired oxygen [FiO_2]). As PH is often secondary to parenchymal lung disease, during period 2, we standardized our approach to PH management focusing on optimizing lung volume and prompt identification and management of secondary contributors to parenchymal lung injury prior to transitioning from inhaled nitric oxide (NO) to chronic PH therapy. Tracheal aspirate samples are sent and virulent organisms (*Staphylococcus aureus*, Gram negative bacteria, and fungus) treated with prolonged antibiotic courses. As part of the management strategy, prophylactic transpyloric feeding tubes were utilized or Nissen fundoplication performed to prevent potential aspiration.^{23–25} In addition, large airway malacia was treated with tracheostomy placement and distending pressure (positive end-expiratory pressure [PEEP]). The presence of airways reactivity and diuretic need were determined with trials of bronchodilators and loop diuretics, respectively. Response to bronchodilator therapy was assessed by decreased peak inspiratory pressure, and hyperinflation on chest X-ray as well as improvement in ventilation and trials of diuretics assessed by evaluating chest X-ray (CXR) changes, and lung compliance in response to therapy. If changes were not seen in lung compliance or CXR, diuretics were discontinued. Addressing these problems is an important initial step in the management of PH. Follow-up echocardiograms were then performed monthly and as needed, with changes in clinical care or condition.

Patients with late PH (defined as a pulmonary artery pressure greater than half the systemic arterial pressure) were reviewed to determine the potential benefits of further studies, such as

cardiac catheterization. Cardiac catheterization provides a more accurate assessment of the severity of PH, and includes acute vasoreactivity testing; assessment of the contribution of shunt lesions such as a patent foramen ovale, atrial septal defect or patent ductus arteriosus; determination of the potential role for left ventricular (LV) diastolic dysfunction, and identification of pulmonary vein stenosis or large collateral vessels.^{26,27} Pulmonary vein stenosis, aorto-pulmonary collaterals, and LV diastolic dysfunction, are complications that occur with increased frequency in infants with BPD,^{26,27} and increase the complexity of the therapeutic decision making options, for treatment of pulmonary arterial hypertension. Pulmonary vasodilator therapy, in this setting, increases pulmonary blood flow and pulmonary edema often ensues. The diagnosis of left ventricular diastolic dysfunction (LVDD) is suspected on echocardiogram, with the presence of left to right atrial level shunting in the presence of elevated right ventricular systolic pressure measured by tricuspid regurgitation jet or indirectly with the presence of septal flattening. LVDD is confirmed at cardiac catheterization with elevated left ventricular end diastolic pressure (<10 mm Hg). LV diastolic dysfunction and poor LV filling is managed with milrinone initially, followed by afterload reduction with angiotensin converting enzyme inhibitors. Use of afterload reduction, improves LV filling and minimizes the development of pulmonary edema, that occurs with pulmonary vasodilator therapy. In the absence of pulmonary vein stenosis and LV diastolic dysfunction, aggressive management of PH is employed, utilizing inhaled NO, sildenafil, and bosentan in refractory cases. All patients with PH were initially treated with inhaled NO, before transitioning to chronic oral therapy. In some instances, initiation of chronic ventilation and addressing contributors to chronic respiratory insufficiency resolved the PH and chronic PH therapy was not indicated. Chronic oral therapy is initially with sildenafil, followed by a combination of sildenafil and bosentan if additional therapy is needed. Use of prostacyclin in this population has been associated with worsening gas exchange secondary to ventilation/perfusion (VQ) mismatch. Pulmonary vein stenosis was managed nonsurgically with intermittent cardiac catheterizations and balloon dilations.

The consequences of aspiration in premature infants with BPD remain poorly understood and whether aggressive treatment of reflux modifies the course remains unclear. With the advent of the VCP, all patients undergoing tracheostomy for chronic ventilation had a gastrostomy tube and a fundoplication performed. This intervention was performed without diagnostic studies to confirm the presence of aspiration, and purely on the basis of having severe BPD. For a small subset of patients, a gastrostomy tube and fundoplication were performed prior to tracheostomy, to determine if aggressive treatment of reflux and preventing aspiration could facilitate extubation.

Data Collection

To compare the demographics and severity of illness between the two periods, 2000 to 2005 and 2006 to 2013, data that was collected included survival, GA at birth, and age at tracheostomy. At the time of tracheostomy, respiratory severity score (RSS; mean airway pressure [MAP] $\times$ FiO₂), the presence of comorbidities, PH, and airway anomalies were also collected. Additional contributing factors were noted including a history of medical complications (necrotizing enterocolitis [NEC], sepsis, ROP, intraventricular hemorrhage [IVH]) and medication usage (pulmonary vasodilators, afterload reducing agents [milrinone,

captopril], diuretics, inhaled and systemic steroids, and mucolytics (DNase). We also recorded long-term outcomes, including the age and cause of death.

Statistical Analysis

All statistical analyses were performed with the Prism software package (v. 5.0a, Graphpad^{Q2}). Nonparametric t-tests and chi-squared analyses were utilized to compare differences in outcomes between study groups. All *p*-values less than 0.05 were considered to be statistically significant.

Results

From 2000 to 2005, 57 patients underwent tracheostomy placement at our institution. Of these 57 patients, 14 had a tracheostomy placed for ventilator-dependent BPD. After establishment of the VCP (from 2006 to 2013), 47 infants have undergone tracheostomy placement, including 27 patients with ventilator-dependent BPD. Comparisons of tracheostomy- and ventilator-dependent infants from these two periods demonstrate no significant difference in GA, gender, RSS, the presence of PH, or the incidence of airway anomalies (Table 3). Patients in period 2 who underwent tracheostomy were slightly older with a greater postconceptional age (Table 3).

There were no differences during period 1 and 2 between the number of patients with NEC, sepsis, ROP needing laser, and severe IVH (grade III or IV). In addition, cardiopulmonary morbidities (PH, LVDD) and respiratory severity (FiO₂, MAP, respiratory severity score, airway anomalies) were not different between the two periods. During period 1, 13 of 14 (93%) infants underwent Nissen fundoplication and during period 2, 27 of 27 (100%) infants underwent Nissen fundoplication. As there was no difference in rate of fundoplication between period 1 and 2, it is unlikely that prevention of reflux and aspiration was responsible for improved survival. Of note, unlike period 1, during period 2, Nissen fundoplication was performed as part of a standardized approach to care.

Despite the lack of difference in cardiorespiratory morbidities at the time of tracheostomy placement, survival was increased from 50% to 85% during period 2 (Fig. 2).

During period 1, 7 of 14 (50%) patients died. Care was withdrawn in three cases, two patients died of sepsis, and two died of progressive respiratory failure. Of the seven patients who died, four had PH. During period 2, 4 of 27 (15%) patients died. Two died when care was withdrawn, one died from progressive respiratory failure, and one did not survive an acute bowel obstruction secondary to adhesions and bowel necrosis. Of these four patients who died, only one had PH.

Medication Usage

During period 1, 7/14 (50%) patients were diagnosed with PH and treated with inhaled NO. Six of fourteen (42.9%) patients underwent cardiac catheterization and 1/14 (6.5%) was diagnosed with pulmonary vein stenosis. Six of these 14 patients (43%) were treated with sildenafil and 3/14 (21%) were treated with a combination of sildenafil and bosentan. In one subject, tracheostomy placement, addressing secondary contributors to lung injury, and

initiating an individualized chronic ventilation strategy eliminated the need for chronic PH therapy. During period 2, 10 of the 27 (37%) patients diagnosed with PH were treated with inhaled NO. Twelve of twenty-seven (44.4%) underwent cardiac catheterization and 3/27 (11.1%) were diagnosed with pulmonary vein stenosis. Two patients without PH underwent cardiac catheterization, one for atrial septal defect closure, and one for pulmonary hemorrhage and coiling of aortapulmonary collaterals. Nine of the 27 patients (33%) were transitioned to sildenafil, and two (7%) were treated with a combination of sildenafil and bosentan. During period 2, in one subject, tracheostomy placement, addressing secondary contributors to lung injury, and initiating an individualized chronic ventilation strategy again prevented the need for further PH medication. Despite the number of patients with PH not being different between groups, 7/14 (50%) versus 10/27 (38%; $p =$ not significant [NS]), mortality among those with PH was markedly greater before the formation of the VCP, 4/7 (56%) versus 1/10 (10%; $p < 0.05$). Of note, all of the patients, 1/1 and 3/3, during periods 1 and 2, respectively, with pulmonary vein stenosis survived.

During period 1, LVDD was present in 2/14 (14%) patients at cardiac catheterization. Both of these infants were treated with milrinone. One of the two was transitioned from milrinone to captopril, but this transition was not tolerated in the second patient (due to hypotension). During period 2, at cardiac catheterization, LVDD was present in 6/27 (22%) patients, five of these six were treated with milrinone and transitioned to captopril. Due to limited IV access, the sixth patient was started on captopril without milrinone.

Medications used to treat PH (inhaled NO, sildenafil, and bosentan) and LVDD (milrinone, captopril) were not different between period 1 and 2. Pulmonary medication use differed significantly between period 1 and 2 with more patients prescribed inhaled steroids 10/14 (71%) versus 5/27 (19%; $p < 0.01$) during period 1, and more systemic steroids (prednisone, 0.5 mg/kg every 48 hours) 0/14 (0%) versus 22/27 (81%; $p < 0.01$) and mucolytic use 0/14 (0%) versus 16/27 (59%; $p < 0.01$) during period 2. Despite an individualized approach and clear criteria for discontinuing diuretics during period 2, there was no difference in diuretic exposure between period 1 and 2 (Table 4). With clear criteria for discontinuing diuretics during period 2, it is likely that duration of exposure to diuretics was shorter during period 2.

Discussion

Despite advances in and improved overall outcomes of extremely premature newborns, a small subset of preterm infants with severe BPD who remain ventilator-dependent beyond term corrected GA persists as a significant clinical challenge. The medical needs of these patients are complex and require the involvement of multiple subspecialists in addition to the primary team. To address the multisystem medical needs of this population, an interdisciplinary VCP was established at our institution based on standardized clinical approaches to respiratory, cardiac, gastrointestinal, nutritional, and neurodevelopmental strategies, as described.

To determine whether such strategies as provided through an organized interdisciplinary program impact the clinical course of infants with severe BPD, we compared survival of infants with ventilator-dependent BPD before and after initiation of this program. We report

a marked improvement in survival to hospital discharge after initiation of the VCP, despite the lack of apparent differences in GA, birth weight, and respiratory status at the time of tracheostomy. While other factors such as differences in medication use (systemic steroids and mucolytics) may account for the improved survival, we attribute this improvement, at least in part, to a greater standardization of care, improved communication among team members and with the family, and the development of a physiology-based approach to chronic respiratory insufficiency and ventilation and the comorbidities of BPD. In addition, differences in medication use and approaches to care, prior to and after the formation of the VCP resulted from improved communication between subspecialists and the primary team, coordinated discussion at the bedside, and a standardized approach to the multifactorial etiologies of respiratory insufficiency in BPD.

VCP consultation originates in the NICU, where the goals of the team are to help assess concerns regarding possible futility, to bridge gaps in knowledge through consistent approaches to BPD-related morbidities, to optimize chronic care in an acute critical care environment, and most importantly, to foster an open environment that facilitates discussion at the bedside. This empowers the nursing staff, subspecialist services, and family caregivers to actively participate in the care of their child. These goals are achieved through inpatient consultation and follow-up, the development of individualized care pathways, weekly bedside rounds, and monthly family conferences. Once stable, infants are transitioned to the pediatric respiratory care unit on the inpatient pulmonary service, where the VCP continues to follow them, providing continuity as arrangements are made for home nursing and durable medical equipment, and as caregivers receive the necessary education and training to ensure a successful transition to home. Outpatient follow-up is through the VCP program in pulmonary clinic, with the pulmonologists on the VCP team responsible for outpatient care. This approach ensures continuity such that the same team follows all patients from the NICU, to discharge and long-term follow-up.

In addition to improved communication and continuity, standardized approaches to respiratory insufficiency and chronic ventilation and aggressive management of the comorbidities that contribute to mortality in severe ventilator-dependent BPD, may have been responsible for improved survival with the VCP. With involvement of the VCP, patients were phenotyped as mentioned previously, and an individualized physiologic approach employed to ventilator management, airway clearance, diuretic, bronchodilator, steroid, and antibiotic use. In general, patients were transitioned from a high-rate, low tidal volume “lung protective” strategy to a more chronic ventilator approach that is aimed at optimizing lung volume and patient–ventilator synchrony, avoiding gas trapping and recurrent atelectasis and to reduce the overall work of breathing.¹⁵ This approach to ventilator support, attenuated signs of respiratory distress, irritability, air hunger, and decreased the need for high levels of sedation. Markers, such as improved interactions with parents and care providers, greater tolerance of physical therapies and routine cares, and fewer episodes of distress and cyanosis with handling or suctioning, become the endpoints of interventions, beyond traditional measures such as blood gas tensions alone. Improved stability and perceptions of greater patient-comfort with mechanical ventilator support is generally very encouraging to the medical staff and care providers, and allows the team to focus on optimizing nutrition and neurocognitive development.

Another contributor to improved survival may be the approach to evaluation and management of PH. Prior reports have demonstrated significant mortality when PH complicates the course in BPD. Survival for infants with severe BPD and PH is $61 \pm 8\%$ at 1 year, and $52 \pm 11\%$ at 2 and 3 years.⁹ During period 1, patients were not screened for PH and the diagnosis made when patients were symptomatic (having episodes of desaturation [spells], after instability with induction of anesthesia, need for high FiO₂). During period 1, 7/14 (50%) of patients were diagnosed with PH and 4/7 (57%) died, consistent with these previously published reports. During period 2, 10/27 (38%) of patients were diagnosed with PH and 1/10 (10%) died. As patients during period 1 were only diagnosed when symptomatic, and not screened for PH, the possibility exists that the rates of PH were underestimated during period 1. Prior reports have demonstrated the presence of PH in 25 to 30% of infants with severe BPD.^{10,11} As the incidence of PH was 50% during period 1, it is unlikely that rates of PH were underestimated. As there was no difference in inhaled NO, sildenafil, and bosentan use between period 1 and 2, other factors are likely responsible for the marked reduction in mortality with PH. Since the development of the VCP, all infants are screened for PH by echocardiogram at 36 weeks GA, increasing the likelihood of earlier detection and management. In addition, as PH is often secondary to parenchymal lung disease, during period 2 prior to initiating chronic therapy, we standardized our initial approach to PH management focusing on prompt identification and management of secondary contributors to parenchymal lung injury and respiratory failure, more specifically, optimizing lung volumes, managing large airways malacia, promoting mucus clearance, addressing small airways reactivity when present, and determining diuretic need. In addition, intercurrent infections and colonization with virulent organisms were treated with prolonged antibiotic courses. While many factors may have contributed to improved survival with PH, we speculate that earlier detection and a standardized approach to secondary contributors to parenchymal lung disease and respiratory insufficiency and precipitants of PH crisis, prior to implementing chronic therapy may be responsible for decreased mortality with PH.

GER complicates the course in premature infants in as many as 60% of infants, and debate exists as to the link between GER and the subsequent development of BPD.^{24,25,28} Aspiration of gastric contents frequently complicates GER; with a recent study demonstrating the presence of pepsin, a marker of gastric contents, in more than 92% of tracheal aspirate samples from premature infants on mechanical ventilation, with significantly higher levels of pepsin in fed infants when compared with unfed infants.²³ Aspiration can exacerbate lung disease and in the setting of severe BPD and PH may have devastating consequences. In our study, between period 1 and 2, aggressive treatment of GER and prevention of aspiration with Nissen fundoplication and gastrostomy tube placement was not different between the 2 periods, making it unlikely that improved survival was secondary to prevention of aspiration. Despite this, published evidence exists that supports routine fundoplication in all infants with significant chronic lung disease, demonstrating dramatic and progressive improvements in respiratory course after fundoplication in selected preterm infants with severe BPD.^{24,25} As our experience mirrors these reports, with many infants weaning from mechanical ventilation and positive pressure ventilation after Nissen fundoplication and other infants demonstrating significant improvements in PH and severity of BPD post Nissen fundoplication, in this subset of

infants with ventilator-dependent BPD, we advocate for early aggressive surgical management of GER with fundoplication and gastrostomy tube placement empirically at the time of tracheostomy placement.

Limitations to our study include the retrospective nature of the study with the use of historical controls. Despite using historical controls, pre-existing morbidities (NEC, sepsis, ROP, IVH) were not different between groups, however, the possibility exists that lack of difference in these comorbidities was due to sample size and that improved survival is secondary to differences in pre-existing morbidities. In addition, the possibility exists that other changes in NICU management (medication use—steroids and mucolytics) may have had some contribution to the differences in outcome. While differences in medication use between the two periods may account for the improved survival, these changes in medical management were secondary to enhanced communication between sub-specialists, nursing and the primary team, and an interdisciplinary approach to care, supporting a programmatic approach to care of these infants. Another limitation to the study is that improved survival may have been secondary to increased tracheostomy placement and decreased withdrawal of support as the age of death was significantly different between the two time periods, 282.2 days (range, 150–441 days) for period 1 versus 422.2 days (range, 176–680 days; $p < 0.01$). During the two periods, cause of death was withdrawal of support for 3/14 (21%) of subjects in period 1 and 2/27 (7%) in period 2. While not statistically different, the possibility exists that pre-existing comorbidities such as NEC, ROP, and IVH may account for a greater percentage of patients in period 1 having support withdrawn and younger age of death. Finally, this analysis was based on outcomes at a single center and may not be generalizable to other centers.

We report that the initiation of a formal interdisciplinary program enhanced the care of infants with severe ventilator-dependent BPD and was associated with improved survival to discharge from 50% to 85%. While changes in management may account for improved survival, formation of the VCP was the basis for these changes, with interdisciplinary discussions and standardized approaches, facilitating decision-making. Our study and prior reports^{7,8} confirm the importance of interdisciplinary teams and programmatic approaches, to optimize management and care for infants with severe ventilator-dependent BPD. Despite improved survival, much remains to be learned from this patient population to optimize late outcomes. Due to the relative infrequency and diverse problems of infants with severe BPD, multicenter collaborative studies²⁹ and evidence-based guidelines are needed to better define strategies, including the role of interdisciplinary teams to enhance long-term cardiopulmonary and neurocognitive outcomes.

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VCP Interdisciplinary Team

- Neonatology and Pulmonology Co-Directors
- Neonatology Primary Team (attending, fellow, NNP)
- Pulmonary Consult Team (attending, fellow, PNP)
- Surgical Subspecialists (as needed)
- Respiratory Therapists
- Nurses (NICU, Inpatient Ward, Clinic)
- Developmental Specialists
- Therapists (Occupation, Physical, Speech)
- Registered Dietitians
- Nurse Case Managers
- Social Work, Child Life Specialist, Chaplain

Fig. 1.
Members of the ventilator care program interdisciplinary team.

	Period 1 2000-2005	Period 2 2006-2013	p Value
Survival	7/14 (50%)	4/27 (85%)	p<0.05
Age of death	Median 282.2 days	Median 422.2 days	p<0.01
	Range (150-441 days)	Range (176-680 days)	

Fig. 2. Survival to hospital discharge was significantly increased after formation of the ventilator care program^{Q3}.

Table 1

Changes in clinical care to address the most common contributors to mortality in our institution

Changes in clinical care after implementation of VCP	
Chronic respiratory insufficiency	Patient specific ventilator approach to multifactorial etiology
	“PEEP” for large airways malacia
	Mucus clearance with saline, bag suctioning, and mucolytics
	Systemic steroids
Pulmonary hypertension	Universal screening at 36 wk PCA
	Optimizing lung volume, prompt identification and management of secondary contributors to parenchymal lung injury, and respiratory failure
Colonization with virulent organisms	Prolonged antibiotic therapy
Reflux and aspiration	Prophylactic transpyloric feeding tubes Routine Nissen fundoplication

Abbreviations: PCA, Patient Controlled Analgesia; PEEP, positive end-expiratory pressure, VCP, ventilator care program.

Table 2

Individualized approach addressing the multifactorial contributors to respiratory failure

Approach to chronic respiratory insufficiency after implementation of VCP					
Heterogeneous parenchymal lung disease	Large airways malacia	Small airways reactivity	Increased mucus production	Pulmonary hypertension	Reflux and aspiration
Tracheostomy placement Volume-guarantee mechanical ventilation	Flexible dynamic bronchoscopy	Bronchodilators	Bag suctioning	Aggressive screening with echocardiogram 36 wk PCA	Routine Nissen fundoplication
High-resolution CT	High PEEP to stent malacia	Oral every other day steroids	Avoid dry suctioning	Trial of diuretics	
Larger tidal volumes (10–12 mL/kg) Low rate (<25 breaths/min) Longer inspiratory times (0.6–0.7 s) Tolerate peak airway pressure (40–50 cm H ₂ O)			Normal saline solution with suctioning Long inspiratory time (0.6–0.7 s) Mucolytics DNase Every other day steroids	Identification/management of contributors to lung injury Infection: tracheal aspirate and prolonged antibiotics Aspiration: transpyloric feeding tube or Nissen fundoplication Large airways obstruction malacia or mucus clearance Small airways reactivity	
Trial of diuretics				Cardiac catheterization	

Abbreviations: CT, computed tomography; PCA, Patient Controlled Analgesia; PEEP, Positive end-expiratory pressure; VCP, ventilator care program.

Table 3

Patient characteristics

	Period 1 (2000–2005)	Period 2 (2006–2013)	<i>p</i> -value
Number of patients	14	27	
Sex	M (7;50%)	M (14; 52%)	NS
	F (7;50%)	F (13; 48%)	
Gestational age	Median (25; 5/7 wk)	Median (26; 5/7 wk)	NS
	(range, 24–28 wk)	(range, 23–33 wk)	
Age at tracheostomy	Median (139 d)	Median (158 d)	<0.05
	(range, 64–246 d)	(range, 74–231 d)	
Postconceptional age at tracheostomy	Median (45; 6/7 wk)	Median (46; 6/7 wk)	<0.05
	(range, 38–61 wk)	(range, 41–71 wk)	
Necrotizing enterocolitis	3/14 (21%)	3/27 (11%)	NS
Sepsis	3/14 (21%)	8/27 (30%)	NS
Retinopathy of prematurity	6/14 (42%)	7/27 (26%)	NS
Intraventricular hemorrhage grade III or IV	2/14 (14%)	2/27 (7%)	NS
Pulmonary hypertension	7 (50%)	10 (38%)	NS
Mortality with PH	4/7 (57%)	1/10 (10%)	<0.05
Left ventricular diastolic dysfunction	2/14 (14%)	6/27 (22%)	NS
FiO ₂	0.40	0.46	NS
Mean airway pressure	11.7	12.9	NS
Respiratory severity score (MAP × FiO ₂)	4.68	5.934	NS
Airway anomalies (tracheo broncho malacia)	7 (50%)	(15) 55%	NS
Nissen fundoplication	13 (93%)	27 (100%)	NS

Abbreviations: FiO₂, fraction of inspired oxygen; MAP, mean airway pressure; PH, pulmonary hypertension; NS, not significant.

Table 4

Differences in medication use (diuretics, steroids inhaled and systemic, bronchodilators, and mucolytics) between period 1 and 2

Medications	Period 1 (2000–2005)	Period 2 (2006–2013)	<i>p</i> -value
Milrinone	2/14 (14%)	5/27 (19%)	NS
Captopril	1/14 (7%)	6/27 (22%)	NS
Inhaled nitric oxide	7/14 (50%)	10/27 (37%)	NS
Sildenafil	6/14 (43%)	9/27 (33%)	NS
Bosentan	3/14 (21%)	2/27 (7%)	NS
Diuretics	18/27 (67%)	9/14 (65%)	NS
Steroids inhaled	10/14 (71%)	5/27 (19%)	<0.01
Steroids systemic	0/14 (0%)	22/27 (81%)	<0.01
Bronchodilators	5/14 (36%)	16/27 (59%)	NS
Mucolytics	0/14 (0%)	16/27 (59%)	<0.01