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Original Article

# Outcomes of infants with severe bronchopulmonary dysplasia in the pediatric intensive care unit

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**Abstract** ***Background*:** Some infants with severe bronchopulmonary dysplasia (sBPD) are referred to higher-level centers for multidisciplinary care, including the pediatric intensive care unit (PICU). However, information regarding these infants is limited in PICUs.

***Methods*:** We investigated the characteristics and outcomes of preterm infants with sBPD referred to the PICU of a tertiary hospital. This retrospective cohort study included 14 preterm infants with sBPD who were transferred to the PICU beyond 40 weeks' postmenstrual age (PMA) because of weaning failure, from January 1, 2014, to September 30, 2018.

***Results*:** The median age at referral was 47.1 weeks (range, 43.6–55.9 weeks), and the median length of stay in the previous neonatal intensive care unit was 154 days (range, 105.8–202.3 days) after birth. After referral the following major comorbidities were found in the patients: large airway malacia, $n = 7$ (50.0%); significant upper airway obstruction, $n = 3$ (21.4%); and pulmonary arterial hypertension, $n = 8$ patients (57.1%). Finally, eight patients (57.1%) were successfully extubated without tracheostomy. Final respiratory support of the patients was determined at a median PMA of 56 weeks (range, 48–63 weeks). Age at referral ($P = 0.023$) and large airway obstruction ($P = 0.028$) were significantly related to a decrease in successful extubation.

***Conclusion*:** Based on a timely and individualized multidisciplinary approach, some of the prolonged ventilator-dependent infants, even those beyond term age, could be successfully extubated.

**Key words** bronchopulmonary dysplasia, mechanical ventilation, pediatric intensive care unit, preterm infants, tracheostomy.

Preterm infants who remain ventilator-dependent beyond term postmenstrual age (PMA) are classified as having severe bronchopulmonary dysplasia (sBPD).[1] This small subset of infants is at an increased risk of several complications.[2] Because of multiple morbidities, they frequently have a complicated disease course and varying disease severity. Thus, the American Thoracic Society published a consensus statement pertaining to the care of sBPD children and emphasized the need for a multidisciplinary approach.[3] Consequently, sBPD infants born in multidisciplinary care-incapable hospitals are referred to higher-level centers.[4] Some children beyond 40 weeks' PMA, could be transferred to the pediatric intensive care unit (PICU), not the neonatal intensive care unit (NICU), because NICU services are usually provided to infants within term age.[5]

sBPD infants who cannot be discharged within 44 weeks' PMA are more likely to continue to receive mechanical ventilation (MV).[6] Therefore, physicians caring for those infants generally focus on attempting to wean infants from MV, rather than focusing on perinatal morbidities, in order to provide care in a less intensive environment as soon as possible. A few reports are available regarding outcomes of sBPD infants who are managed in the NICU.[6,7] However, since infants in the early phase of sBPD are transferred to the NICU at a younger age, PICU physicians are expected to have more experience with older infants with established sBPD. Additionally, based on the reports of consistent prevalence of sBPD compared to increased survival of preterm infants,[7] such transfer of sBPD patients will further increase the PICU workload. However, reports describing sBPD infants transferred to the PICU are few because of the low incidence at any single center.

This study aimed to investigate the characteristics and overall outcomes of ventilator-dependent sBPD patients who were transferred to the PICU beyond 40 weeks' PMA, and to identify predictors of successful extubation in this population.

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## Methods

### *Data sources and eligibility criteria*

This retrospective cohort study included all infants transferred to the PICU of Seoul National University Children's Hospital from NICUs because of weaning or extubation failure, from January 1, 2014 to September 30, 2018. Since regionalization of NICU is not established in South Korea,[8] infants over term age are referred to PICUs at the request of NICU physicians or parents. Our PICU received a total of 46 infants from 27 NICUs across the country during the study period. Among them, we enrolled infants born at <32 weeks' gestation who had sBPD, defined as receiving either a fraction of inspired oxygen ($FiO_{2)} \geq 0.30$ or positive pressure ventilation (PPV) at 36 weeks' PMA or at the time of referral, whichever came later.[1]

Our exclusion criteria were (i) gestational age ≥32 weeks; (ii) diagnosis of combined major congenital anomalies or neuromuscular diseases, such CHARGE [coloboma, heart defect, atresia choanae (also known as choanal atresia), restricted growth and development, genital abnormality, and ear abnormality] syndrome, cri-du-chat syndrome, achondroplasia, DiGeorge syndrome, VACTERL [vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities] syndrome, imperforated anus, congenital mitral stenosis, congenital myopathy, congenital myotonic dystrophy, and myotubular myopathy; (iii) a tracheostomy prior to referral and suspicion of upper airway obstruction (UAO) without sBPD; and (iv) transfer to another hospital while undergoing treatment in our hospital (Data S1).

### *Individualized and multifactorial approach to causes of chronic respiratory failure in sBPD*

Our tertiary hospital, with a 24-bed PICU, frequently receives referrals from NICUs or PICUs nationwide, because of extubation or weaning failure. Based on previous reviews on management,[9–11] including ventilator strategies, we developed a multidisciplinary approach protocol for the causes of weaning failure in sBPD and applied this protocol to sBPD infants (Data S2).

### *Independent variables*

All medical records from the previous hospital that were uploaded to the electronic medical records of our hospital were reviewed for perinatal characteristics, including gestational age at birth, birthweight, sex, and history of neonatal morbidities, such as surgical neonatal enterocolitis, intraventricular hemorrhage, patent ductus arteriosus ligation operation, retinopathy of prematurity requiring laser operation, pulmonary arterial hypertension (PAH), and any cardiopulmonary resuscitation before referral. Any history of infection resulting from a pathogen proven by microbiological studies within 7 days before referral, was reviewed.

Data at referral were collected from medical records and included body weight, head circumference, feeding status, use of medications (i.e., corticosteroids, inotropic agents, antibiotics, intravenous sedative drugs, anti-PAH medications), need for MV, and results of venous or capillary blood gas analyses. To characterize the severity of the lung disease at referral, we used the oxygen saturation index (OSI) and ventilation index (VI). In recent clinical studies, the OSI has been validated in PICU and NICU patients as a reliable index for assessing severity of respiratory failure and lung injury.[12,13] Furthermore, it can be utilized instead of the oxygenation index when arterial blood assessment is not feasible. The VI is also a widely used index, as it incorporates a factor measuring the intensity of therapy in patients with respiratory failure.[14] Individual OSI and VI were calculated from the data when ventilator settings were stabilized within 1 day of referral, to avoid reflecting any sudden exacerbation immediately after transfer, as follows: $OSI = \text{mean airway pressure} \times FiO_2 \times 100 \div SpO_2$, $VI = PCO_2 \times \text{peak airway pressure} \times \text{respiratory rate}/1{,}000$. In addition, severity at referral was estimated by the predicted mortality rate using the prediction algorithm of the Pediatric Risk of Mortality IV score.[15]

Medical records, for progress and outcomes after referral to the PICU were also reviewed. To determine respiratory comorbidities after referral, special investigations were performed, such as a chest computed tomography (CT), flexible bronchoscopy, and rigid bronchoscopy. Based on the results, airway problems combined with sBPD were reported by dividing them into large airway obstruction (LAO) (i.e., tracheo- and/or bronchomalacia) and UAO (i.e., subglottic stenosis, laryngeal edema, formation of granulation tissue, vocal cord palsy). Echocardiography was performed by a pediatric cardiologist who documented what the cardiac problem was. PFO was differentiated from atrial septal defect (ASD) depending on whether flaps were seen overlapping the fossa ovalis and the presence of a tunnel-like defect, rather than a true defect within the septum. Echocardiography documentation of PAH, based on elevated right ventricular systolic pressure, direction of shunting, or flattening of the septum, were collected. The type and duration of medications administered in the PICU were reviewed, including corticosteroids, intravenous sedation, anti-PAH drugs, antihypertensive drugs, intravenous antibiotics, and inotropes.

### *Outcomes*

The primary outcome was successful extubation and the timing of final respiratory support (FRS). FRS for sBPD infants was defined as any medical device for respiratory assistance, which was determined after referral and maintained until PICU discharge. The timing of FRS was the date of successful extubation or the date of tracheostomy, expressed in weeks' PMA. Additionally, we reported survival prior to discharge and PICU length of stay.

### Ethics

Institutional review board approval (IRB No. H-1807-014-955) was obtained for this study on July 9, 2018 with a waiver for informed consent from patients.

### Statistical analysis

Continuous nonparametric data were presented as median (interquartile range, IQR), whereas categorical variables were expressed as number and percentage. Since our cohort was relatively small and the timing of FRS was varied, we used Cox proportional hazard models for identifying predictors of successful extubation. Clinical factors (before, after, and at referral) associated with MV dependency were analyzed. Continuous variables were not categorized, since using the cut-offs would result in low numbers of patients in specific categories and unstable models. Statistically significant variables ($P < 0.1$) with univariate analyses were included in the multivariate Cox proportional hazard model using backward stepwise regression. The final multivariate results were presented as hazard ratios (HR) and their 95% confidence intervals (CI). Significance in multivariate analysis was defined as a $P < 0.05$ and the assumption of proportionality was verified graphically using long-log survival plots. The correlation between the timing of FRS and clinical factors was analyzed using the Spearman's bivariate correlation test or the Mann-Whitney $U$ test, depending on the variables. All tests were two-tailed. Data were analyzed using IBM SPSS software, version 21 (IBM, Armonk NY).

## Results

### General characteristics and clinical outcomes of sBPD infants requiring prolonged MV in the PICU

During the study period, 14 patients were eligible for analysis. The clinical characteristics at birth, before referral, and at referral are presented in Table 1. The median gestational age and birthweight were 26 weeks (IQR 25–29 weeks) and 875 g (IQR 642.5–955.0 g), respectively. Patients were transferred to the PICU at a median age of 154 days (IQR 105.8–202.3 days) and at 47.1 weeks' PMA (43.6–55.9 weeks). At referral, two patients were transferred without MV. However, it was confirmed that they were still dependent on MV immediately after transfer, therefore MV was re-applied to them. The median OSI and VI scores were 4.2 (IQR 2.7–6.9) and 46.3 (IQR 27.5–77.2), respectively.

The outcomes after referral are also presented in Table 1. After referral, the FRS of each patient was individually determined at a median PMA of 56.7 weeks (IQR 48.4–63.7 weeks) and at a median of 43.5 hospital days (IQR 25.8–85.5 days). Of the 14 patients, six (42.9%) underwent tracheostomies, of whom one patient died after tracheostomy placement, but prior to discharge from the PICU. However, despite autopsy, the cause of this sudden patient death was not identified. Eligible infants stayed in the PICU for a median of 66 days (IQR 47.3–92.0 days) at the first admission.

**Table 1** General characteristics and clinical outcomes of sBPD infants requiring prolonged mechanical ventilation in the pediatric intensive care unit

| Characteristics | Median (IQR) or $n$ (%), $n$ = 14 |
|---|---|
| Age at referral (days) | 154 (105.8–202.3) |
| PMA at referral (weeks) | 47.1 (43.6–55.9) |
| Male | 9 (64.3) |
| Birth characteristics | |
| Gestational age at birth (weeks) | 26.7 (25.3–29.0) |
| Birth body weight (g) | 875.0 (642.5–955.0) |
| Neonatal morbidities before referral | |
| PDA ligation operation | 8 (57.1) |
| Pulmonary arterial hypertension | 7 (50.0) |
| ROP operation | 4 (28.6) |
| Surgical NEC | 3 (21.4) |
| High grade IVH (III/IV) | 1 (7.1) |
| Medical conditions at referral | |
| Body weight (<3rd percentile) | 3 (21.4) |
| Head circumference (<3rd percentile) | 10 (71.4) |
| Full enteral feeding | 10 (71.4) |
| Recent pathogen proven infection† | 0 (0.0) |
| Mechanical ventilation at referral | 12 (85.7) |
| Oxygen saturation index | 4.2 (2.7–6.9) |
| Ventilation index | 46.3 (27.5–77.2) |
| Predicted mortality rate (%)† | 2.7 (1.4–3.7) |
| Outcomes | |
| Tracheostomy | 6 (42.9) |
| PMA at which final respiratory support was determined (weeks) | 56.7 (48.4–63.7) |
| Hospital days when final respiratory support was determined | 43.5 (25.8–85.5) |
| PICU length of stay (days) | 66 (47.3–92.0) |
| Mortality | 1 (7.1) |

†Any infections resulting from pathogen proven by microbiologic studies within 7 days before referral. ‡Predicted mortality rate is calculated based on Pediatric Risk of Mortality IV. IQR, interquartile range; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PICU, pediatric intensive care unit; PMA, postmenstrual age; ROP, retinopathy of prematurity; sBPD, severe bronchopulmonary dysplasia.

### Results of evaluation and management of sBPD infants after referral to the PICU

Evaluation and management results after referral for each patient are shown in Table 2. sBPD infants showed a heterogeneous phenotype of the respiratory system. LAO was commonly identified in seven patients (patients 6, 7, 8, 9, 11, 12, and 13) on chest CT and/or bronchoscopy. LAO was mostly identified as tracheo- or bronchomalacia, and airway compression by an aberrant right subclavian artery, requiring angioplasty, was also found in patient 6. Additionally, three of the eight patients who required anti-PAH drugs had newly identified PAH or needed additional anti-PAH medications (patients

**Table 2** Results of evaluation and management of sBPD infants with prolonged ventilation after referral to the pediatric intensive care unit ($n$ = 14)

| Patient | Major comorbidities combined with BPD | | Several comprehensive managements for successful extubation | | | | | Outcomes | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Airway | Heart | PAH medication | Corticosteroid use [§] | NAVA mode | Extubation attempts [¶] | Others | FRS determination PMA (weeks) | Hospital days of FRS determination | FRS at discharge |
| 1 | | PFO | N | N | N | 1 | | 42.4 | 18 | NP |
| 2 | | PAH, ASD | Y | N | N | 1 | | 43.3 | 7 | NP |
| 3 | | PFO | N | N | N | 1 | Ileostomy repair | 44.1 | 22 | NP |
| 4 | | | N | Y | N | 3 | | 49.9 | 29 | NP |
| 5 | | PAH, ASD | Y | Y | Y | 1 | | 53.9 | 48 | HFNC |
| 6 | LAO[†], UAO | | N | Y | Y | 1 | Angioplasty | 55.3 | 82 | T/HV |
| 7 | LAO | PAH | Y | Y | N | 1 | | 56.4 | 64 | NP |
| 8 | LAO | PAH, PFO | Y | N | Y | 1 | | 57.0 | 80 | NP |
| 9 | LAO, UAO | | N | N | Y | 0 | | 58.7 | 27 | T/HV |
| 10 | | PAH, PFO | Y | N | Y | 1 | | 63.3 | 52 | NP |
| 11 | LAO, | PAH, PFO | Y[†] | N | Y | 0 | | 63.3 | 39 | T/HV |
| 12 | LAO, UAO | PAH, ASD | Y | Y | Y | 1 | Inguinal hernia repair | 65.0 | 64 | T/HV |
| 13 | LAO | | N | Y | Y | 3 | | 65.3 | 89 | Dead |
| 14 | | PAH, PFO | Y[†] | N | N | 1 | | 85.4 | 30 | T/HV |

†LAO due to external compression by the right subclavian artery. [‡]Patients who added PAH medication after transfer. [§]Corticosteroid use includes usage during the weaning period for more than 7 days and excludes usage for the short period of extubation. [¶]Only includes planned extubation. AI, adrenal insufficiency; ASD, atrial septal defect; FRS, final respiratory support; LAO, large airway obstruction; NAVA, neurally adjusted ventilatory assist; NP, nasal prong; PAH, pulmonary arterial hypertension; PFO, patent foramen ovale; PMA, postmenstrual age; sBPD, severe bronchopulmonary dysplasia; T/HV, tracheostomy with home ventilation; UAO, upper airway obstruction.

7, 11, and 14) after referral. A total of six patients received corticosteroids under the subjective judgment of the attending physician for weaning, and half of them (patients 4, 5, and 7) were responsive enough to achieve successful extubation. Extubation was attempted in 12 patients; however, in the remaining two patients (patient 9, 11), tracheostomy was undertaken without an extubation trial.

### *Predictors of successful extubation in sBPD infants*

Table 3 presents the variables that were statistically correlated with successful extubation. In the univariate analysis, previous NICU length of stay, no requirement of MV at referral, and absence of LAO were correlated with higher rates of successful extubation. However, no statistical correlation was observed with successful extubation and other clinical variables, including perinatal morbidities and higher VI/OSI at referral (Data S1). A Cox regression model applied to the multivariate analysis showed a negative relationship between successful extubation and longer stay in previous NICU (HR 0.93, 95% CI: 0.86–0.99; $P$ = 0.023) and presence of LAO (HR 0.01, 95% CI: 0.00–0.62; $P$ = 0.028). The proportion of the patients without successful extubation by age at referral and LAO is shown in Fig 1.

The timing of FRS was positively correlated with the length of previous NICU stay ($r$ = 0.91, $P$ < 0.001), but there was no statistically significant association between the timing of FRS and the length of PICU until FRS determination ($r$ = 0.57, $P$ = 0.28). There were statistically significant differences in the timing of FRS according to groups as follows ($P$ = 0.012): successful extubation, median 51.9 weeks (IQR 43.7–56.7 weeks); tracheostomy 64.1 weeks (57.9–64.1 weeks).

## Discussion

To our knowledge, this study is the first to report the characteristics and outcomes of sBPD infants who were transferred to the PICU and had prolonged MV dependency.

**Table 3** Predictors of successful extubation in sBPD infants ($n = 8$)

| Clinical characteristics | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *P*-value | HR | 95% CI | *P*-value |
| Extubation trial more than 3 times at previous NICU | 3.69 | 0.86–15.78 | 0.075 | | | |
| Previous NICU length of stay (days) | 0.97 | 0.94–0.99 | 0.007 | 0.93 | 0.86–0.99 | 0.023 |
| Mechanical ventilation at referral | 0.13 | 0.02–0.94 | 0.043 | | | |
| Large airway obstruction | 0.19 | 0.04–0.95 | 0.043 | 0.01 | 0.000–0.62 | 0.028 |
| Duration of sedation after referral | 0.94 | 0.88–1.01 | 0.075 | | | |

CI, confidence interval; HR, hazard ratio; NICU, neonatal intensive care unit; sBPD, severe bronchopulmonary dysplasia.

We found that a small cohort of sBPD infants who were transferred to the PICU due to long-term MV dependency had various phenotypes requiring customized management, with about half of these patients having been successfully extubated. sBPD infants undergoing unusual courses are likely to be dependent on MV for a prolonged period.[6] Therefore, to be discharged from the intensive care unit, MV weaning is an important task. However, if MV support is not sufficiently reduced in a short time, physicians consider switching from the use of conventional MV in ICU to home MV that can be used in a general ward and at home. This might have to be preceded with tracheostomy in some cases.[16–19]

In our study, infants with longer previous NICU stays were likely to have a decreased possibility of successful extubation and to delay the FRS decision. Age at referral directly reflects the intubation period and prolonged intubation is a well-known risk factor of extubation failure in all age groups. Longer NICU stay is also related to a more complex course, including adverse clinical events.[6] Although each perinatal comorbidity was not related to successful extubation in this study, we assume that small events, not well described and documented before referral, could lead to a longer NICU stay. Since a systematic approach to prolonged MV dependency was conducted after transfer, age at referral can also be considered a reflection of the timing of FRS planning. Thus, a timely approach to chronic respiratory failure itself could finally lead to successful extubation and early decision-making regarding FRS in sBPD infants with protracted MV.

The second predictor of successful extubation was the absence of LAO. In sBPD infants, severe chronic lung disease and PPV result in tracheo- and/or bronchomalacia, which explains why PPV is constantly required to reduce dynamic airway collapse.[20] Of note, respiratory severity was not correlated with successful extubation. This result might indicate that successful extubation cannot be predicted by accessing only the lungs, because the cause of MV dependency is multifactorial in this patient group.[2] Thus, in patients with chronic respiratory failure, as well as sBPD infants, understanding the various respiratory phenotypes and comorbidities is a key step for management, including tailored ventilator care.[2,9–11] To identify factors that potentially cause prolonged MV dependency, multiple modalities could be attempted.[2,21] In general, problems in the airway are dynamically observed by bronchoscopy, which is already proven safe in infants.[22] A chest CT is also informative, not only to evaluate BPD severity, but also to detect structural abnormalities.[23] In our study, we were able to provide a comprehensive and individualized plan for sBPD infants depending on the phenotypes identified. For example, aortopexy was performed to relieve atypical LAO,

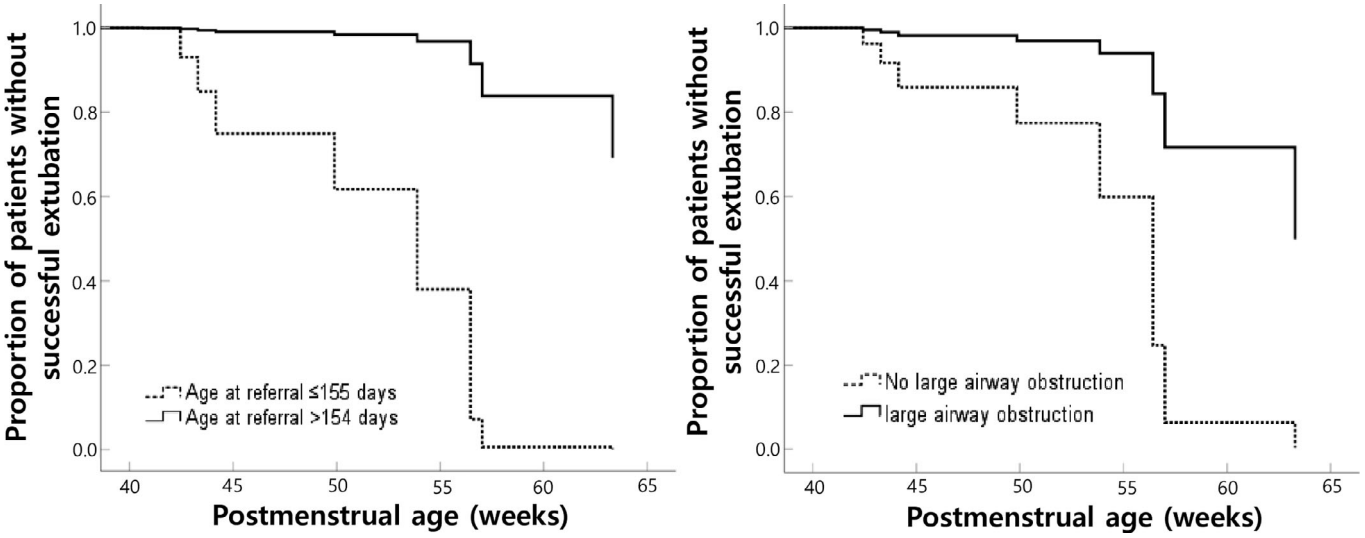


**Fig 1** The cumulative probability curves of independent predictors of successful extubation. (a) Patients are divided into two groups by age at referral with median age of 154 days. Difference in rates of successful extubation between older and younger patients at referral ($P = 0.023$). (b) Difference in rates of successful extubation between patients with and without large airway obstruction ($P = 0.028$).

early tracheostomy was determined for severe UAO without delay, and anti-PAH medications were added for newly diagnosed or worse PAH. Thus, the results of this study highlight the consideration of extensive evaluations and change of management direction at some point in sBPD infants who do not respond to general management.[2,21]

Timely determination of whether successful extubation is possible without delay is the ultimate goal in PICU. However, it is difficult for families and clinicians to accept extubation failure and decide on tracheostomy placement for their child, with its multiple advantages and disadvantages. In recent studies, it has been reported that earlier tracheostomy may not only allow for an earlier transition to home ventilation, shorter hospital stay, and earlier oral feeding, but also lead to better neurodevelopmental outcomes.[24,25] On the other hand, tracheostomy may result in accidents and a socioeconomic burden on the family.[25] Moreover, tracheostomy timing is reported to be unrelated to outcomes in preterm infants.[19] Therefore, it is postulated that, because of uncertainty, the FRS decision was delayed in infants who underwent tracheostomy, compared to infants who achieved successful extubation in this study.

To date, no specific recommendation is available about the optimal timing for tracheostomy for sBPD. Furthermore, tracheostomy timing varies considerably between centers (between 40–50 weeks' PMA) because of variations in clinician practice.[17–19,26] Recently, it has been suggested that a tracheostomy should be considered at near term in PMA, when there is no significant improvement despite respiratory support.[27] However, in our study, whether tracheostomy was required or not was determined at a PMA of 56.7 weeks, which is fairly late, with only 3% of sBPD infants are hospitalized.[6] Interestingly, half of our patients finally achieved successful extubation, and this result may be due to our comprehensive approach and personalized management. Therefore, in contrast to decisions based on specific time periods in preterm infants, tracheostomy placement should be individualized in this population. Nevertheless, because a low probability of successful extubation was observed after 60 weeks' PMA of with favorable factors, our findings suggest that tracheostomy placement should be considered within that age. Additionally, in terms of neurodevelopment and UAO concerns, previous studies[24,25] have recommended that timing could be brought forward, depending on the comorbidities. Further research including more cases is required, but to our knowledge, this study is the first to report the significant success rate of extubation in sBPD infants after referral to PICU.

Our study had some limitations. First, it included a small number of patients in a single hospital, thus, generalization of our results may be limited. As sBPD infants transferred to the PICU account for a small population in a single center, a multicenter study is required to obtain more information. Second, there could be selection bias because some of the sBPD patients stayed in the NICU beyond term age without being transferred to the PICU. However, considering that preterm infants born at < 32 weeks' gestation are discharged from the NICU at an average of 44.0 weeks of PMA in South Korea,[28] and the infants in our study were transferred to the PICU at a median age of 47.1 weeks' PMA, the number of infants who stayed in the NICU, especially after 44 weeks, would be very small. Therefore, it is estimated that the selection bias had a minimal effect on this study. Third, multiple efforts to wean infants from MV could lead to delayed timing of the FRS decision; however, no statistical correlation was found between PICU length of stay after referral and timing of the FRS decision. Fourth, because this is a retrospective study conducted at a referral hospital, some clinical events that occurred in the NICU may not have been recorded in the reports from previous NICUs. Nevertheless, we speculated that previous events are unlikely to actively influence the status at referral. Thus, we thoroughly reviewed the records of patients for medical conditions that might affect MV dependency at the time of referral and investigated this relationship. Finally, the gap between the day of tracheostomy placement and the day the decision was made by the intensivist could have led to age overestimation at the FRS decision, but it would not be significant as the gap was within 1 week.

In conclusion, whether successful extubation is possible in sBPD with prolonged MV dependency over term age is the key concern at the bedside for clinicians. We found that younger age at referral (reflection of intubation period, complex course in NICU, and the timing of multi-systematic evaluation) and absence of LAO is related with successful extubation in this population in PICU. Based on the evaluation and individualized management, some of the sBPD infants could additionally achieve successful extubation even beyond the average age previously reported. This information may aid PICU physicians caring for sBPD infants transferred to the PICU in deciding long-term respiratory support.

## Disclosure

The authors declare no conflicts of interest.

## Author contribution

Y.H.C designed the study, performed the acquisition and analysis of the data, and drafted the manuscript. H.Y.A. and Y.S.K. collected data and reviewed/revised the manuscript. J.D.P. conceptualized and designed the study, and critically reviewed the manuscript. All authors read and approved the final manuscript.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Data S1. Study population flow chart.

Data S2. Multidisciplinary approach to the causes of chronic respiratory failure in severe bronchopulmonary dysplasia.