Official title Clinical Characteristics and Outcomes Until 2 Years of Age in Preterm Infants With Typical Chest Imaging Findings of Bronchopulmonary Dysplasia: A Propensity Score Analysis

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Bronchopulmonary dysplasia (BPD) is a common chronic respiratory disease in preterm infants. The increase in the survival rate of premature babies following the improvement of perinatal treatment and care has caused an increase in the incidence of BPD in recent years, which has seriously affected the quality of life of preterm infants. According to the consensus reached at the workshop sponsored by the National Institute of Child Health and Human Development (NICHD) in 2001 , BPD was clinically defined based on oxygen dependency in preterm infants. However, the refined NICHD definition of BPD in 2018 emphasized imaging findings to support a diagnosis of lung parenchyma disease.

Fibrotic opacities and cystic changes on chest imaging [chest X-ray (CXR) or computed tomography (CT) scan] were considered typical findings in BPD patients. In patients with severe BPD, the presence of bubbles/cystic appearance on CXR after 28 days of life was reported to be an important factor, and typical imaging findings can predict a poor pulmonary outcome in BPD patients. BPD is associated with poor outcomes. Although many studies have been conducted on BPD, there are limited reports specifically evaluating the association of typical imaging findings with clinical characteristics and later outcomes in patients with BPD.

We hypothesized that BPD with typical imaging findings was likely to be a particular subgroup of this entity, with a unique etiology, clinical characteristics and prognosis. Therefore, we performed a retrospective cohort study using data from the Department of Neonatology, Children's Hospital of Chongqing Medical University (CHCMU), and the patients were followed by telephone. Eligible patients fulfilled the following three criteria simultaneously: (1) BPD diagnosis according to the 2001 NICHD consensus; (2) chest imaging examination (CXR or CT) in the first week after birth; and (3) hospitalization within the first 7 days after birth. Patients were excluded from the study if they met one of the following conditions: (1) major congenital malformations or laboratory-confirmed chromosomal abnormalities; (2) inadequate clinical data or missing chest imaging data; or (3) loss to follow-up.

Relevant data were retrospectively collected, including demographics [i.e., sex, gestational age, age at admission, birth weight (BW)], perinatal factors [i.e., pregnancy induced hypertension (PIH), CAM, cesarean section, prenatal glucocorticoid administration, respiratory distress syndrome (RDS), sepsis, PDA, 5-min Apgar score], management during hospitalization [i.e., surfactant administration, noninvasive and invasive mechanical ventilation (IMV), postnatal

glucocorticoid administration, packed red blood cell (PRBC) transfusion], complications during hospitalization [i.e., IVH, retinopathy of prematurity (ROP), NEC], and outcomes. Primary outcomes were the severity of BPD, HOT at discharge, and mortality between 28 days after birth and 2 years of age. Secondary outcomes were (1) duration of hospital stay; (2) duration of oxygen supplementation; (3) routine physical assessment; (4) wheezing disorders; and (5) clinical visits and rehospitalizations for a respiratory reason between discharge and follow-up. The long-term outcomes were evaluated until 2 years of age.

Statistical Analysis

Statistical analysis was performed using SPSS 26.0. We used the Shapiro-Wilk test to analyze the normality of the data distribution. Variables without normal distributions were analyzed using the Wilcoxon-Mann-Whitney test and are reported as medians [interquartile ranges (IQRs)]. All normally distributed variables were analyzed using a t-test for comparisons of two independent groups and are presented as the means ± standard deviations. Categorical variables were analyzed using the chi-square test or Fisher's exact tests and are reported as the numbers (%) of subjects. To further evaluate the associations between typical chest imaging findings and the primary and secondary outcomes, a propensity score analysis with 1:1 matching was performed. The following covariates were included based on previous studies: GA, BW, cesarean section, CAM, PIH, sepsis, RDS, PDA, prenatal glucocorticoid administration, postnatal glucocorticoid administration, NEC, IVH, RSD, IMV ≥ 7 days, ≥2 PRBC transfusions. The nearest neighbor matching method was used to select each matched pair by using calipers with a width equal to 0.01 of the standard deviation of the logit of the propensity score. Typical chest imaging findings and the above 15 covariates were analyzed for collinearity and incorporated into the multivariate binary regression model, and the forward likelihood ratio (LR) was used to select the variables to further determine the independent factors of BPD infant mortality. A p-value < 0.05 was considered statistically significant.