Predictors of Bronchopulmonary Dysplasia

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KEYWORDS

• Bronchopulmonary dysplasia • Predictors/risk factors • Chronic lung disease
• Mechanical ventilation

KEY POINTS

- Bronchopulmonary dysplasia (BPD), also called chronic lung disease, is the most common serious pulmonary morbidity in premature infants.
- Premature infants with BPD have lifelong morbidities, including an increased risk of cerebral palsy and mental retardation.
- The incidence of BPD is inversely related to gestational age and birth weight.
- Prediction of BPD using parsimonious models by postnatal day is now possible.

INTRODUCTION

Although significant advances in respiratory care have been made in neonatal medicine, bronchopulmonary dysplasia (BPD) remains the most common serious pulmonary morbidity in premature infants. Premature infants with BPD have a longer initial hospitalization than their peers without BPD.[1] BPD remains a substantial lifelong burden. The costs of the disorder are both social and economic, and are measured in impaired childhood health and quality of life, family stress, economic hardship, and increased health care costs.[2–4]

Over the past 40 years, the definition, disease, and risk factors for BPD have changed.[5,6] BPD, as it was initially described by Northway and colleagues[7] in the 1960s, was based on clinical and radiographic evidence of pulmonary disease in moderately to late premature infants with a history of respiratory distress syndrome. The respiratory management of

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these infants included exposure to prolonged mechanical ventilation and oxygen exposure. On histologic samples, the characteristic areas of hyperinflation alternating with areas of focal collapse were often noted, and hyperplasia of the bronchial epithelium.[8] Radiography of these infants showed areas of heterogeneity throughout the lung fields and coarse scattered opacities in the most severely affected of infants.[9]

The classical BPD described by Northway and colleagues has been replaced by a milder form of the disease. There is reason to believe that risk factors associated with the "new" BPD, compared with historical risk factors, may be distinct. This new BPD occurs in less mature infants exposed to antenatal steroids, who are often treated with exogenous surfactant therapy. They spend fewer days on positive pressure ventilation and have less exposure to supplemental oxygen. Animal studies suggest that the histology of new BPD shows more diffuse disease, fewer areas of hyperinflation, and a reduction in alveoli and capillaries, but little fibrosis.[10,11]

The incidence of BPD varies widely between centers, even after adjusting for potential risk factors. Data from 2010 from the Vermont Oxford Network show that the rates of BPD vary from 12% to 32% among infants born at less than 32 weeks' gestation. Although multiple trials have been aimed at reducing the incidence of BPD, the incidence seems to be stagnant, or even increasing. The rising absolute number of infants with BPD might be caused by the improvement in the survival of extremely low gestational age infants, the population most likely to have this diagnosis.[5,12,13] Compared with the pathology described by Northway and colleagues, the most common type of BPD today may be a less severe form of the disease.

This article reviews the definitions of BPD and the predictors of BPD by time period (before, at, and after birth). Several of the estimators that are available to quantify the risk of BPD, and to explain how this might affect clinicians, families, and researchers, are also reviewed.

DEFINING BPD

The definition of BPD most often uses receipt of oxygen therapy or positive pressure for a duration of time (usually in days) or on a specific day (eg, postnatal day 28 or at postmenstrual age [PMA] 36 weeks). The original definition was based on receipt of oxygen at 28 days of age. However, this definition does not take into account the various developmental considerations of infants born across the spectrum of susceptible gestational ages. Thus, attempts have been made to improve the definition through a corrected age "cut point," most commonly the need for supplemental oxygen therapy at 36 weeks' PMA. The National Institute of Child Health & Human Development (NICHD) divided the definition further using a severity scale. Because oxygen saturation targets vary among centers, a "physiologic definition" also has been proposed. These definitions are reviewed in more detail later.

A workshop to clarify the definition of BPD was held by the NICHD in June 2000 with the goal of distinguishing BPD from chronic lung disease (CLD), a condition that was believed to represent a group of heterogeneous diseases occurring later in life.[14] This workshop proposed a severity-based definition that classified BPD as mild, moderate, or severe based on either postnatal age or PMA (**Table 1**). Mild BPD was defined as a need for supplemental oxygen throughout the first 28 days but not at 36 weeks' PMA or at discharge; moderate BPD as a requirement for oxygen throughout the first 28 days plus treatment with less than 30% oxygen at 36 weeks' PMA; severe BPD as a requirement for oxygen throughout the first 28 days plus 30% oxygen or greater and/or positive pressure at 36 weeks' PMA. Ehrenkranz and colleagues[15] validated the NICHD severity-based definition of BPD through comparing it with the more traditional