Bronchopulmonary Dysplasia: The Trigger of Future Lung Function Decline

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The association between preterm birth and adult health is becoming increasingly recognized.[1] With recent improvements in treatment for neonatal care, overall mortality declined among extremely premature infants.[2] Survival increased most markedly for infants born between 22 and 24 weeks' gestation, and survival without major morbidity increased for infants aged 25 to 28 weeks.[3,4] However, the prevalence of neonatal chronic lung disease, known as bronchopulmonary dysplasia (BPD), has not diminished and rather increased, unlike other morbidities complicating severe prematurity.[3-6]

Northway et al. first characterized BPD 50 years ago, now termed "classic BPD", as a chronic pulmonary disorder occurring in preterm infants with severe respiratory distress syndrome who had been exposed to mechanical ventilation and oxygen supplementation.[7] In the postsurfactant era, BPD is characterized by persistent decreases in alveolar counts, with enlarged alveoli, leaving an overall reduction in the surface area available for gas exchange. Thus, it is considered a consequence of disrupted or arrested lung development, defined by the need for supplemental oxygen at 36 weeks' corrected gestational age.[8] Most preterm infants with BPD have structural lung abnormalities and impaired ventilatory function, consequently raising risk for persistent and severe respiratory morbidity early in life.[9,10] Mean length of hospitalization for those born under 1000 grams is approximately 60 days with high rates of need for additional medical support, including rehospitalization after discharge.[11] During their first year of life, 49% of infants with BPD require rehospitalization, and mortality risks associated with pulmonary complications of BPD are significant.[12,13] Respiratory morbidity tend to be worse in children with severe lung function abnormalities.[14] On the other hand, symptoms progressively subside over time, respiratory exacerbations become uncommon, and most people lead seemingly normal lives.[7,15] Recent intriguing data from ^{3}helium MRI studies suggest that the deranged alveolar development seen after preterm delivery might be compensated in the first decade of life, possibly as a result of late alveolarisation.[16]

Compared to fullterm control subjects, survivors of BPD have impaired respiratory function, which causes consistently reduced airflow due to substantial airway obstruction and alveolar hyperinflation across all age groups.[17,18] This difference was less apparent when comparing children born prematurely with BPD to those born prematurely without BPD. The degree of airflow limitation in the first year of life seems to predict later pulmonary function.[19] Survivors of BPD may have functional abnormalities including airway hyperresponsiveness[20] and reduced exercise performance due to impaired ventilatory adaptation and reduced gas transfer.[21]

Lung abnormalities that might persist into adulthood include airway obstruction, airway hyperreactivity and emphysema.[7,22–24] Long-term outcomes of BPD are difficult to characterize, as adults currently available for study represent survivors of outdated care. However, there is concern that preterm infants may be susceptible to chronic obstructive pulmonary disease (COPD) in later life.[7,25] Hyperoxic insults to the immature lung might cause smooth muscle hyperplasia, airway remodelling,[26] and reprogramming of innate immunoregulatory pathways in the lung.[27] This is known to reduce resistance to respiratory infections and increase risk of COPD. Additional longitudinal studies are necessary to determine outcomes beyond the second decade, and define risk factors and optimal treatment for late sequelae of disease.

Reduced airway function identified soon after birth might predispose to wheezing and reduced lung function in later life.[28] Other important predictors of adult respiratory morbidity are lower respiratory tract illnesses and reduced airway function or airway hyperresponsiveness in early life, which are known as outcomes of BPD.[29] Children with persistent asthma with reduced growth of lung function are at increased risk for fixed airflow obstruction and possibly COPD in early adulthood.[30] Furthermore, a substantial proportion of deficits in lung function in the third decade of life, especially in individuals with asthma, has been reported to persist into late adulthood and might predispose to COPD.[31] Taken together, there might be a complex association between BPD, deficits in early life airway function, lower respiratory tract illnesses, asthma, and COPD.[32]

In conclusion, BPD can no longer be considered as just a pediatric disease. For some infants born prematurely, especially those with BPD, substantial obstructive lung disease persists into adolescence and young adulthood. This pulmonary derangement remains latent in most people, but a reduced respiratory reserve could increase the risk of a COPD-like phenotypes later in life. Because many premature infants are now approaching adulthood, physicians should investigate prenatal/perinatal history, recognize lung disease that is potentially associated with prematurity and other early life insults, and offer long-term monitoring.

References

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