Editorial Commentary

Lung function in adults born prematurely with bronchopulmonary dysplasia

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Bronchopulmonary dysplasia (BPD), which interferes pulmonary vascular and alveolar development especially in preterm infants, usually results from hyperopia, degree of prematurity, prolonged mechanical ventilation and other antenatal risk factors. The diagnostic criteria for BPD are persistent oxygen dependency up to 28 days of life and/or a need for supplemental oxygen at the postmenstrual age of 36 weeks (1).

Infants with BPD may not only suffer respiratory-related problems such as respiratory distress symptoms, increased bronchial secretion and repeated lower tract infection, but also develop feeding problem and delayed growth. Systemic hypertension, poor neurodevelopmental outcome, pulmonary hypertension and left ventricular hypertrophy and left ventricular dysfunction are complications attributed to BPD (2). BPD survivors may also be at a greater susceptibility of developing compromised lung defence, asthma-like symptoms and exercise intolerance for long term (3).

The study by Yang *et al.* (4) in the issue of Paediatrics conducted a national cohort study to investigate the alterations in lung function (i.e., spirometry, plethysmographic lung volumes, diffusing capacity and single-breath nitrogen washout). They described those very low birth weight (VLBW) survivors aged 26–30 years (born in 1986) in New Zealand suffered higher incidence of airflow obstruction, gas trapping, reduced gas exchange and ventilator inhomogeneity. Moreover, BPD (defined as receiving supplementary oxygen at 36 weeks' postmenstrual age) worsened the scenario. These findings suggested BPD have long-term effects on lung function and raise awareness that late pulmonary sequelae might lead to higher occurrence of pulmonary diseases in future years.

Indeed, a considerable body of data has revealed that BPD might contribute to the deviations in lung function. Preterm infants with BPD had diminished functional residual capacity (FRC) depending on severity of the disease (5,6) and compliance (6). Extremely preterm infants with BPD at a post-conceptional age of 44 weeks had airway obstruction measured by lower peak tidal expiratory flow as a proportion of expiratory time (TPTEF/TE ratio) reflected the increasing severity of BPD (7). Infants with BPD at the age of 36–42 postconceptional weeks had reduced respiratory functions demonstrated by higher incidence of concave tidal breathing flow-volume loop (TBFVL) and an increased respiratory rate (8). Furthermore, survivors with BPD had abnormal airway patency in the first year (9) and third year (10) of life measured by decreasing maximal flow at FRC (V'maxFRC). VLBW preterm infants with BPD also had lower forced vital capacity (FVC) (11), forced

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expiratory flow at 50% of vital capacity (FEF50) (11), forced expiratory volume in one second (FEV_1) (11-13), and forced mid-expiratory flow (FEF25–75) (12,13) but increased residual volume/total lung capacity (RV/TLC) ratio (14) at school age. Impaired lung function caused by BPD appears to persist into not only childhood but also adolescence. A diminished FEV_1/FVC of BPD survivors was observed in late adolescence (15). Furthermore, alterations in airway hyperresponsive, diffuse capacity, lung and chest wall mechanics, ventilation inhomogeneity and exhaled nitric oxide have been observed in infancy, preschool age and childhood (16). Yang *et al.* (4) then reported that adult VLBW survivors especially those with BPD had a higher incidence of airflow obstruction, gas trapping, reduced gas exchange, and increased ventilatory inhomogeneity versus controls. BPD might have negative effects continuously on lung function at adults.

However, ventilation strategies used in 1986 were quite different from now. Lung-protective ventilation (i.e., moderate PEEP, low inspiratory pressure, low tidal volume and short inspiratory time) is commonly used now in order to prevent volutrauma, barotrauma and lung inflammation which are potential risk factors to BPD. Non-invasive ventilation (i.e., nasal continuous positive airway pressure, nasal intermittent positive pressure ventilation, nasal high-frequency oscillatory ventilation etc.) is also preferred to invasive ventilation in preterm neonates as it helps increase survival rate without BPD. Non-invasive ventilation should be able to ensure maintenance of FRC, prevent cyclical re-opening and closing, support fatigable ventilatory muscles and provide respiratory stimulation, thereby improving gaseous exchange. Intubation and mechanical ventilation of preterm infants remains the critical factors of subsequent BPD (17). Since Yang's study only mentioned numbers of participants and days of assisted ventilation via an endotracheal tube, we couldn't tell whether this would affect the number of participants diagnosed as BPD under different respiratory support strategy.

A better definition of BPD diagnostic criteria was addressed in 2000: oxygen need for ≥28 days and at 36 weeks' postmenstrual age to identify different severity of BPD, and also to include oxygen concentration at 36 weeks' postmenstrual age to further define the severity of lung injury. Therefore, the number of preterm infants diagnosed as BPD in Yang's study may be different according to the new diagnostic criteria, which in turns affecting the results (1).

In addition to invasive mechanical ventilation exposure, surfactant deficiency in the immature lung or surfactant dysfunction due to oxidant injury and lung inflammation are contributing factors to the pathogenesis of BPD. Although late administration of exogenous surfactant did not reduce the incidence of BPD (18), early surfactant therapy helped reduce the need for aggressive ventilation strategies, thereby preventing BPD (19). It also has been recommended to use non-invasive ventilation strategies and less invasive surfactant administration/minimally invasive surfactant administration (LISA/MIST) whenever feasible for BPD prevention (20). Exogenous surfactant therapy was not used on those participants Yang's study recruited, which may affect results and cannot reflect current condition.

Despite the difference of clinical management between past and present mentioned previously, Yang's study demonstrated the long-term adverse effects of BPD on lung function and raise awareness to those survivors to keep tracking their lung function throughout life and avoid potential exacerbating risk factors. Neonatologists and respiratory therapists thus should work on reducing incidence of BPD in very preterm infants by applying and closely monitoring appropriate respiratory support strategy and medical intervention, thereby preventing short-term and long-term impacts on human health in their future life.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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