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Title: Decreased variability of expired CO2 yield in infants with bronchopulmonary dysplasia

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Body: Background: Bronchopulmonary dysplasia (BPD) is characterized by alterations in ventilation-to-perfusion (V/Q) matching and gas exchange capacity. The aim of this study was to examine the breath-by-breath variability in the expired CO2 volume (VCO2) and to assess its value in describing disturbances of gas exchange in BPD. Methods: Lung function parameters from 181 healthy infants (128 term, 53 preterm) and 87 infants with BPD (46 mild, 55 moderate, 32 severe) were compared. Expiratory capnograms were obtained by mainstream capnography over 100 consecutive tidal breaths. The ratio of VCO2 to expiratory volume (Ve) was used as measure of the expired CO2 yield per breath. The tho-dimensional (2D) domain area of the VCO2/Ve embedding plot (1-breath lag) and the domain area of the VCO2-Ve scatter plot (both calculated by an ellipse-fiting method) were used as indicators of the variability in CO2 yield. Results: BPD infants had smaller 2D VCO2/Ve domains (median [IQR]: 7.8 [4.9-11.6] vs. 10.6 [7.1-15.3]; P<0.001] and VCO2-Ve domain areas (4.0 [2.6-6.2] vs. 7.4 [5.3-10.8]; P<0.001). BPD was a significant determinant of the domain areas independently of Ve and respiratory rate. The discriminatory ability (ROC curve analysis) of the domain area of the VCO2-Ve plot (AUC 0.796 [0.744-0.849]) was significantly higher than that of the 2D domain of the VCO2/Ve embedding plot (0.722 [0.665-0.774) and that of the LCI (0.589 [0.528-0.646]). Conclusions: Infants with BPD presented significantly lower breath-by-breath variability in CO2 yield, a finding that may reflect disease-related disturbances in V/Q matching and gas exchange capacity.