Response to dexamethasone predicts diagnosis of severe (type 2) bronchopulmonary dysplasia or death

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Response to Dexamethasone Predicts Diagnosis of Severe (type 2) Bronchopulmonary Dysplasia or Death
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Background
Bronchopulmonary dysplasia (BPD) is the most common respiratory morbidity after preterm birth but requires diagnosis near corrected full-term age. Postnatal dexamethasone is often used to improve lung function. Yet objective measures of steroid response remain lacking. An understanding of steroid response holds significant promise as a surrogate endpoint for new therapies.

Objective
To create a quantitative measure of clinical response following Dexamethasone administration and association to downstream BPD classification at 36-weeks.

Design/Methods
• A retrospective chart review was performed of preterm infants treated with the DART protocol at Children’s Mercy’s Level IV NICU 2010-2020
• Data (Table) was collected at key timepoints (Day 1, 3, 7) for each infant
  o Ventilation mode was defined as either high frequency oscillatory, conventional invasive, or any form of non-invasive support. Highest daily mode was recorded.
  o Support level was measured by respiratory severity score (RSS= MAP*FiO2).
• BPD outcomes were defined according to the 2017 BPD Collaborative definition.
  o Composite of mild, moderate, or severe (type 1) BPD was used as referent group to assess odds against severe (type 2) BPD or death.
• A regularized logistic model was fitted and resulting predicted probabilities were divided into quartiles to obtain a discrete risk level (level 1 to 4).

Results
• Study cohort included 94 infants with complete ventilatory and blood gas data and who completed a DART course prior to 36-week BPD assessment.
  • A 10,000-iteration bootstrap was performed. A risk score was predicted for infants not included in the resampled data at each iteration and the proportion of those with severe (type 2) BPD or death at each level was evaluated (Figure).
    o For comparison, predictions were also made with a baseline model using only demographic and steroid detail data.
• Increasing risk category was well aligned with rising outcome incidence, ranging from ~20% of infants at level 1 to ~55% of infants at level 4.

Conclusions
• Changes in ventilatory parameters over the course of dexamethasone administration improved BPD prediction compared to baseline demographics alone.
• Incorporating drug response phenotype into a BPD model may enable more rapid development of future therapeutics.

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