Variability in Blood Gas Levels During Non-Invasive Ventilatory Support Following Planned Extubation and Association to 36-Week Bronchopulmonary Dysplasia in Preterm Neonates

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IRB Number: 11120563

Describe role of Submitting/Presenting Trainee in this project (limit 150 words): (150/150)

While this project is still ongoing, Michele has contributed in large part to its development and in several stages to obtain this preliminary data.

First, together with two other KCUMB Students, Michelle helped perform multiple rounds of validation for the automated methodology needed to extract NIV intervals used as the basis of this work. This involved a) extensive review of temporal data, matching indices for extubations and intubations from those produced by the routine (review of multiple clinical parameters) b) development of rules to better capture extubated events for those misaligned windows.

Second, she played an important role in developing the study question. This has involved weekly meeting with our research group to perform a) initial review of data and identify potential physiologic variables for evaluation b) literature review to support their selection. She has also been engaged with Brooke Smith (respiratory therapy) to align feature selection with clinical implications.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words (499/500)

Background:

Despite shifts to non-invasive support, as of 2012, 87% of preterm infants admitted to the neonatal intensive care unit (NICU) continued to receive some form of invasive mechanical ventilation[1]. As a result, research around how prolonged respiratory support may impact the development of chronic lung disease, specifically bronchopulmonary dysplasia (BPD) has flourished. To date, literature has established associations between the time on invasive mechanical ventilation and incidence BPD[2,3]. Resulting in the development of standardized extubation strategies and bringing with them objective measures of extubation readiness[4,5]. Yet, due to their volatile conditions, some neonates will inevitably need to be reintubated. Given the established risk of invasive ventilation, the decision of when to do so, varies widely between care teams; integrating patient's physiologic state and physician's experience. Stemming from this lack of standardization, patient conditions vary widely before reintubation, and it remains unclear if the degree of deterioration in infant's physiologic state during periods of non-invasive ventilatory support (NIV) may also be associated with downstream lung injury. Quantifying such associations may serve to guide evidence-based practice for future reintubation guidelines.

Objective:

The objective of this study was to determine the association between variability in premature infants' physiologic state prior to reintubation and BPD classification at 36-weeks. A secondary objective aimed to identify empirical deterioration thresholds to provide risk-based guidance for reintubation.

Data & Analysis:

Data were retrospectively drawn from the Children's Hospitals Neonatal Database (CHND) and electronic medical records (EMR) of infants admitted to Children's Mercy NICU 2010-2016. Inclusion criteria required infants to be preterm, admitted within three days of life, and intubated within one day post-admission. Infants must also have been intentionally extubated and subsequently reintubated prior to 36-weeks, those with multiple extubations before 36-weeks were excluded. BPD status at 36-weeks was classified per the CHND; and grouped into (None/Mild-BPD) and (Severe-BPD/Death) for analysis.

Automated methodology for extracting periods of NIV support from EMR data was developed and validated on a random 30 infants (~5%). For each infant, timestamped data was extracted, including measures of respiratory support (FiO2) and physiologic measurements (blood gases, respiratory rate, SpO2). Bayesian logistic regression was used to estimate the magnitude and directionality of association between NIV measurements and BPD outcomes. Models were adjusted for known confounders, including demographics (gestational age, birthweight, sex, race), use of surfactant or antenatal steroids, and timing (extubation day of life, hours extubated, and time reintubated before assessment).

Results:

All infants with complete data were utilized, resulting in a cohort of 124. Beyond known relationships to BPD (e.g., sex, length of time reintubated), we identified novel associations between the maximal and minimal values of blood gas measures during NIV, and BPD Outcomes. Complete results can be found in Table 1.

Conclusions:

This work offers a first step to understanding how patient deterioration during NIV may be associated with longer-term outcomes. Future work includes more comprehensive characterization of NIV blood gas trajectories, and exploration into high-risk thresholds. Understanding these relationships may aid in standardization of reintubation strategies to improve patient morbidity.

	Mean	SD	HDI 2.5%	HDI 97.5%
Sex – Female (Reference: Male)	0.11	2.07	0.03	0.46
Race – Black (Reference: White)	0.89	2.02	0.23	3.62
Race – Other (Reference: White)	1.35	3.15	0.15	12.82
Antenatal Steroids – Yes (Reference: No)	1.32	1.88	0.38	4.53
Surfactant – Yes (Reference: No)	1.16	1.88	0.33	4.03
Reintubation Time – ≥155hr (Reference <155hr)	5.30	1.97	1.38	19.57
GA – Extremely Preterm (Reference: Preterm)	0.09	3.17	0.01	0.79
*Birthweight_T**	0.75	1.08	0.64	0.87
*Extubated Day Post-Admission _T**	1.26	1.26	0.81	2.05
*Hours Extubated_T**	1.00	1.01	0.99	1.01
PCO2 Min Value	1.20	1.08	1.05	1.40
HGB Min Value	0.42	1.31	0.24	0.69
SpO2 Min Value	1.02	1.02	0.98	1.07
PH Min Value	0.00	555.02	0.00	22.00
PCO2 Max Value	0.94	1.04	0.87	1.02
HGB Max Value	1.67	1.28	1.01	2.70
SpO2 Max Value	0.36	1.42	0.18	0.70
PH Max Value	1.85E+06	2.18E+04	5.39E-03	5.19E+14

Table 1: Results of the Bayesian Regression. Estimated Means represent an Odds Ratio per 1 unit increase (continuous data) or between indicated level and reference level (categorical data). HDI (High Density Interval), Bayesian equivalent to a confidence interval), 2.5% represents the lower bound, 97.5% represents the upper bound of the 95% interval. Those features marked with _T were transformed with a square root function to account for model assumptions.*

References:

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4. Gupta, Dhruv, et al. "A predictive model for extubation readiness in extremely preterm infants." *Journal of Perinatology* 39.12 (2019): 1663-1669.
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