

Project 2: Regression Analysis

Github Link

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Abstract

This study talks about the development and comparison of various regression models to predict the necessity and timing of tracheostomy placement in infants diagnosed with severe Bronchopulmonary Dysplasia (BPD). Utilizing a rich multi-center dataset from BPD Collaborative Registry, this project examined an array of demographic and clinical variables to identify significant predictors of tracheostomy or death. Our findings indicate that lower birth metrics and the need for ventilation support at critical postmenstrual ages are closely associated with higher tracheostomy rates and mortality. The models' performance, particularly the mixed-effects model, highlighted the random variability across different medical centers, suggesting the need for a nuanced approach in clinical decision-making. Despite demonstrating robust predictive power, the models' limitations stem from untested logistic regression assumptions such as linearity, the impact of outliers, and multicollinearity. These limitations highlight areas for future research and model optimization to enhance predictive accuracy and clinical utility. The results underscore the complexity of managing severe BPD and the potential for regression models to inform clinical strategies to improve patient outcomes.

1. Introduction

Bronchopulmonary dysplasia (BPD) is the most common and one of the prognostically significant consequence of premature birth, affecting between 10,000 and 15,000 infants in the United States each year (Jensen and Schmidt 2014). Despite advances in understanding its pathophysiology and the development of management strategies aimed at reducing its occurrence, the incidence of BPD has remained unchanged over the years (Stoll et al. 2015). In cases of severe BPD, particularly Grade 3 (defined by 2001 NHLBI criteria), which requires ventilator dependence at 36 weeks of corrected gestational age, about 75% of these infants still need ventilator support upon hospital discharge, although not permanently. Tracheostomy, which is necessary for 2-4% of infants with BPD and up to 12% of those with severe or Grade 3 BPD, has several benefits such as stable airway maintenance, improved growth, and enhanced age-appropriate interactions. Early tracheostomy within four months, is associated with better outcomes, with infants receiving this procedure earlier (before 120 days) showing lower risks of death or neurodevelopmental impairment at 18-22 months (DeMauro et al. 2014). However, there is still no consensus on the optimal timing for tracheostomy. Previous studies utilizing large databases have successfully predicted the likelihood of tracheostomy or death using basic demographics and clinical diagnosis. However, these studies lacked detailed respiratory data and did not offer predictions at varying postmenstrual ages (PMA).

This project aims to create a regression model to predict the composite outcome of tracheostomy or death, thus guiding to determine the criteria and optimal timing for tracheostomy. Several models will be discussed and compared, including mixed-effect model, best subset selection, and lasso regression and ridge regression.

2. Data

2.1. Data sources

The data comes from the BPD Collaborative Registry, a multi-center consortium of interdisciplinary BPD programs located in the United States and Sweden formed to address gaps in evidence and promote research to enhance the care of children with severe forms of BPD. It specifically records data on infants born before 32 weeks of gestation and diagnosed with severe bronchopulmonary dysplasia (sBPD), as defined by the 2001 NHLBI criteria. This includes infants requiring a fractional inspired oxygen (FiO₂) of more than 0.3 or any form of positive pressure ventilation at 36 weeks postmenstrual age (PMA). The registry gathers standard demographic and clinical information at key intervals: at birth, and at 36, 44 weeks PMA, and at discharge.

The data is pre-processed by converting the variables into the appropriate types as specified in the codebook. Out of 28 variables, 26 have missing values. Missing values in the variable of **center** are imputed based on the patients' record IDs. Three duplicate records have also been removed. Since **mat_race** is recorded differently between the data and the codebook, this variable will be excluded from future analyses.

Table 1 presents the challenge of missing data across various variables, with the extent of missingness showing significant variation. Notably, data collected at the 44-week corrected gestational age exhibit the most substantial missingness. Additionally, the variable **any_surf**, indicating surfactant administration within the first 72 hours, displays a similar pattern of missingness to the 44-week variables. A significant number of missing entries are also found in the 36-week data. To address these concerns, multiple imputation will be implemented to enable a more robust and complete analysis.

Table 1: Summary of Missing Values

Variable	Number	Pct	Variable	Number	Pct
inspired_oxygen.44	451	45.15%	blength	78	7.81%
p_delta.44	451	45.15%	birth_hc	77	7.71%
weight_today.44	449	44.94%	mat_chorio	62	6.21%
peep_cm_h2o_modified.44	449	44.94%	mat_ethn	57	5.71%
any_surf	433	43.34%	mat_race	56	5.61%
ventilation_support_level_modified.44	427	42.74%	prenat_ster	35	3.5%
med_ph.44	427	42.74%	ventilation_support_level.36	30	3%
com_prenat_ster	193	19.32%	med_ph.36	30	3%
p_delta.36	128	12.81%	sga	15	1.5%
hosp_dc_ga	124	12.41%	center	10	1%
peep_cm_h2o_modified.36	117	11.71%	gender	4	0.4%
weight_today.36	92	9.21%	del_method	3	0.3%
inspired_oxygen.36	92	9.21%	Death	2	0.2%

2.2. Demographics and Clinical Diagnosis

Table 2 highlights the variability in tracheostomy rates and mortality rates among the centers. The tracheostomy rates has a range from 0% at Center 20 to 100% at Center 21, underscoring the significant disparities in practice. Notably, Centers 12 and 1 exhibit higher rates of 50.72% and 41.54%, respectively, which may suggest more aggressive treatment approaches or patient profiles requiring such interventions. In contrast, Centers 3, 7, and 16 have rates below 4%, which could reflect variations in demographics, protocols, or resources. The mortality rates ranges from 0% at Center 7, 16, 20 and 21 to 20.29% at Center 12. The incidence of death is more rare compared to tracheostomy.

The pronounced differences across centers are statistically confirmed by a chi-squared test ($p < 0.001$). Importantly, Center 2 accounts for over 60% of the patient cohort, highlighting a multilevel data structure

and underscoring the importance of appropriately accounting for the `center` variable in analysis.

Table 2: Tracheostomy and death Proportions across the Centers

Center	Total	Tracheostomy Proportion	Death Proportion
1	65	41.54%	10.77%
2	630	10.16%	4.60%
3	57	1.75%	1.75%
4	60	18.33%	1.67%
5	40	12.50%	5.00%
7	32	3.12%	0.00%
12	69	50.72%	20.29%
16	38	2.63%	0.00%
20	4	0.00%	0.00%
21	1	100.00%	0.00%

The demographic and clinical diagnosis data presented in Table 3 compare infants across different tracheostomy statuses and mortality outcomes, revealing noteworthy differences in several metrics.

For tracheostomy cases, there was a notable reduction in birth weight compared to those without tracheostomy, with a median weight of 655 grams versus 753 grams, respectively, and this difference was statistically significant with a p-value of 0.04. Additionally, 30% of the infants in the tracheostomy group were small for gestational age (SGA), a higher percentage than the 19% in the non-tracheostomy group ($p=0.005$). Delivery method differed significantly, with more infants in the tracheostomy group born via cesarean section (79% vs. 70%, $p=0.035$). A significant contrast was evident at 36 weeks of corrected gestational age, with 72% of the tracheostomy group requiring invasive positive pressure ventilation, compared to 20% not needing such support ($p<0.001$) in the no tracheostomy group. By 44 weeks, the need for invasive positive pressure increased to 77% in the tracheostomy group versus just 15% ($p<0.001$). The no tracheostomy group’s non-invasive positive pressure decrease from 67% at 36 weeks to 28% at 44 weeks, while the tracheostomy group only dropped 7%. Additionally, infants with tracheostomies have higher median peak inspiratory pressures at both 36 and 44 weeks, and a greater proportion required medication for pulmonary hypertension at 44 weeks. The tracheostomy group also had significantly higher discharge ages. Mortality rates were significantly higher in the tracheostomy group (12% vs. 4.4%, $p<0.001$), suggesting that infants requiring tracheostomy may have more severe underlying conditions or complications. No significant differences were observed in maternal ethnicity, chorioamnionitis, or gender.

In terms of death, the number of deceased infants totaled 54, which is fewer than the 146 requiring tracheostomy. Similar patterns are observed. The median birth weight in the group that passed away was significantly lower at 603 grams compared to 750 grams in the surviving group, with a small p-value of less than 0.001, and a greater proportion of these infants were categorized as SGA (48% versus 19%, $p<0.001$), highlighting a more pronounced disparity. However, the delivery method did not show a significant difference here. At 36 weeks’ corrected gestational age, the requirement for invasive positive pressure was much higher in the mortality group (81%) compared to the living group (24%), with a significant p-value of less than 0.001. At 44 weeks, the need rose to 85% in the mortality group versus 23% in the living group ($p<0.001$). The reduction in non-invasive positive pressure use was steeper in the living group, falling from 64% at 36 weeks to 26% at 44 weeks, whereas the mortality group only has a negligible decrease of 2%. Those in the mortality group also had significantly later discharge ages. Rates of tracheostomy were markedly higher in the mortality group (31% versus 14%, $p<0.001$), reinforcing the notion that tracheostomy is often associated with more severe health complications. Similar to the tracheostomy analysis, no significant differences were noted in maternal ethnicity, chorioamnionitis, or gender.

Table 3: Demographics and Clinical Diagnosis in Infants

Characteristic	Tracheostomy			Death		
	No Tracheostomy, N = 850	Tracheostomy, N = 146	p-value	No, N = 940	Yes, N = 54	p-value
center						
1	38 (4.5%)	27 (18%)		58 (6.2%)	7 (13%)	
2	566 (67%)	64 (44%)		600 (64%)	29 (54%)	
3	56 (6.6%)	1 (0.7%)		56 (6.0%)	1 (1.9%)	
4	49 (5.8%)	11 (7.5%)		58 (6.2%)	1 (1.9%)	
5	35 (4.1%)	5 (3.4%)		38 (4.0%)	2 (3.7%)	
7	31 (3.6%)	1 (0.7%)		32 (3.4%)	0 (0%)	
12	34 (4.0%)	35 (24%)		55 (5.9%)	14 (26%)	
16	37 (4.4%)	1 (0.7%)		38 (4.0%)	0 (0%)	
20	4 (0.5%)	0 (0%)		4 (0.4%)	0 (0%)	
21	0 (0%)	1 (0.7%)		1 (0.1%)	0 (0%)	
Maternal Ethnicity			0.3			0.8
Hispanic or Latino	66 (8.2%)	8 (5.9%)		71 (8.0%)	3 (5.9%)	
Not Hispanic or Latino	737 (92%)	128 (94%)		815 (92%)	48 (94%)	
Birth Weight (g)	753 (606, 950)	685 (560, 870)	0.004	750 (605, 940)	603 (474, 790)	<0.001
Obstetrical Gestational Age						
Birth Length (cm)	25 (24, 27)	25 (24, 27)	0.7	25 (24, 27)	26 (24, 27)	0.8
Birth Head Hircumference (cm)	32 (30, 35)	31 (29, 34)	0.15	32 (30, 35)	29 (27, 33)	<0.001
Delivery Method			0.12	23.00 (21.50, 25.00)	21.50 (20.50, 24.00)	0.003
Vaginal delivery			0.035			0.090
Cesarean section	254 (30%)	31 (21%)		274 (29%)	10 (19%)	
Prenatal Corticosteroids	594 (70%)	114 (79%)		663 (71%)	44 (81%)	
Complete Prenatal Steroids	712 (86%)	123 (94%)	0.011	789 (87%)	44 (90%)	0.5
Maternal Chorioamnionitis	524 (76%)	86 (76%)	>0.9	574 (76%)	34 (79%)	0.6
Gender	138 (17%)	22 (16%)	0.8	153 (17%)	7 (14%)	0.5
Female			>0.9			0.14
Male	348 (41%)	60 (41%)		390 (42%)	17 (31%)	
Small for Gestational Age	498 (59%)	86 (59%)		546 (58%)	37 (69%)	
Not SGA			0.005			<0.001
SGA	678 (81%)	100 (70%)		748 (81%)	28 (52%)	
Received Surfactant	161 (19%)	42 (30%)		177 (19%)	26 (48%)	
Weight at 36 Weeks	395 (81%)	66 (88%)	0.14	433 (82%)	28 (88%)	0.4
Ventilation Support at 36 Weeks	2,140 (1,864, 2,405)	2,030 (1,793, 2,289)	0.025	2,140 (1,870, 2,400)	1,760 (1,320, 2,030)	<0.001
No respiratory support or supplemental oxygen			<0.001			<0.001
Non-invasive positive pressure	111 (13%)	6 (4.7%)		114 (12%)	2 (4.2%)	
Invasive positive pressure	560 (67%)	29 (23%)		582 (64%)	7 (15%)	
Fraction of Inspired Oxygen at 36 Weeks	168 (20%)	92 (72%)		220 (24%)	39 (81%)	
Peak Inspiratory Pressure (cm H2O) at 36 Weeks	0.30 (0.23, 0.35)	0.45 (0.35, 0.60)	<0.001	0.30 (0.23, 0.37)	0.50 (0.34, 0.60)	<0.001
Positive and Exploratory Pressure (cm H2O) at 36 Weeks	0 (0, 0)	14 (2, 23)	<0.001	0 (0, 2)	16 (11, 26)	<0.001
Medication for Pulmonary Hypertension at 36 Weeks	7 (6, 8)	8 (6, 9)	<0.001	7 (6, 8)	8 (6, 8)	0.073
Weight at 44 Weeks	41 (4.9%)	25 (20%)	<0.001	55 (6.0%)	10 (21%)	<0.001
Ventilation Support at 44 Weeks	3,730 (3,260, 4,130)	3,630 (3,163, 4,015)	0.2	3,740 (3,288, 4,130)	3,245 (2,640, 3,723)	<0.001
No respiratory support or supplemental oxygen			<0.001			<0.001
Non-invasive positive pressure	262 (57%)	7 (6.3%)		268 (50%)	1 (2.6%)	
Invasive positive pressure	128 (28%)	18 (16%)		141 (26%)	5 (13%)	
Fraction of Inspired Oxygen at 44 Weeks	71 (15%)	86 (77%)		124 (23%)	33 (85%)	
Peak Inspiratory Pressure (cm H2O) at 44 Weeks	0.28 (0.25, 0.32)	0.39 (0.30, 0.58)	<0.001	0.28 (0.25, 0.35)	0.53 (0.32, 0.67)	<0.001
Positive and Exploratory Pressure (cm H2O) at 44 Weeks	0 (0, 0)	18 (9, 37)	<0.001	0 (0, 2)	27 (16, 43)	<0.001
Medication for Pulmonary Hypertension at 44 Weeks	0 (0, 8)	8 (8, 10)	<0.001	0 (0, 8)	8 (8, 9)	<0.001
Hospital Discharge Gestational Age	48 (10%)	51 (46%)	<0.001	75 (14%)	24 (62%)	<0.001
Death	45 (42, 52)	72 (55, 100)	<0.001	46 (42, 54)	53 (44, 65)	0.012
Trach	37 (4.4%)	17 (12%)	<0.001			
No Tracheostomy				811 (86%)	37 (69%)	<0.001
Tracheostomy				129 (14%)	17 (31%)	

¹ n (%); Median (IQR)² Pearson's Chi-squared test; Wilcoxon rank sum test³ Fisher's exact test; Wilcoxon rank sum test; Pearson's Chi-squared test

3. Methods

3.1. Multiple Imputation

Multiple imputation will be used to address missing data. This method creates several imputed datasets, introducing variability in the imputed values to reflect the uncertainty around the true values. The imputation phase involves applying algorithms repetitively to generate values for the missing data. Subsequently, in the analysis phase, each dataset undergoes standard statistical analysis as though it were complete. The final phase, pooling, aggregates the results from all datasets, yielding parameter estimates that incorporate the variability across the imputations. In our project, models are fitted to 5 complete datasets, and the resulting estimates are then pooled, thus derivating final models.

3.2. Models

In this project, four models are compared: logistic mixed-effect model with the **center** variable as a random effect, best subset selection, lasso regression, and ridge regression. Both 5-fold cross-validation and train-test splitting methods will be employed for building models. The model will be trained on 70% of the data and validated on the rest data.

Mixed-effect model incorporates fixed effects for the observed covariates and random effects for the intercepts associated with each center, capturing the variability between centers. The mixed-effects approach is particularly suited for data where random variability exists across different groups—in our study, medical centers. The penalized form for the mixed-effects model would be:

$$\underset{\beta, b}{\text{minimize}} \|Y - X\beta - Zb\|_2^2 + \lambda \|b\|_2$$

where Z is the random effects design matrix, b is the random effects and $\|\beta\|_2 = \sum_{j=1}^p \beta_j^2$.

With a response vector $Y \in \mathbf{R}^n$, predictor matrix $X \in \mathbf{R}^{n \times p}$ and a subset size k between 0 and $\min\{n, p\}$, best subset selection aims to identify the set of k predictors that minimize the squared error, solving the nonconvex problem

$$\underset{\beta \in \mathbf{R}^p}{\text{minimize}} \|Y - X\beta\|_2^2 \quad \text{subject to} \quad \|\beta\|_0 \leq k,$$

with $\|\beta\|_0 = \sum_{i=1}^p 1\{\beta_i \neq 0\}$ denoting the count of nonzero entries in β , known as the ℓ_0 norm.

The lasso method solved a convex relaxation of the best subset by replacing the ℓ_0 norm with the ℓ_1 norm,

$$\underset{\beta \in \mathbf{R}^p}{\text{minimize}} \|Y - X\beta\|_2^2 \quad \text{subject to} \quad \|\beta\|_1 \leq t,$$

where $\|\beta\|_1 = \sum_{i=1}^p |\beta_i|$ and $t \geq 0$ is a tuning parameter, which can be also commonly represented in a penalized form

$$\underset{\beta \in \mathbf{R}^p}{\text{minimize}} \|Y - X\beta\|_2^2 + \lambda \|\beta\|_1,$$

where now $\lambda \geq 0$ serves as a tuning parameter.

On the other hand, the ridge method minimize

$$\underset{\beta \in \mathbf{R}^p}{\text{minimize}} \|Y - X\beta\|_2^2 + \lambda \|\beta\|_2.$$

The only difference between these two regularization regressions is their penalty terms. Both best subset and lasso can help us to perform variable selection.

The project's aim is to construct a regression model that predicts the combined outcome of tracheostomy or death. This model will inform the criteria and optimal timing for tracheostomy placement. Consequently, we introduce a new composite variable, Y . In this binary outcome, patients are labeled '1' if they received a tracheostomy or succumbed to their condition, and '0' if they survived without undergoing a tracheostomy. This variable allows for a comprehensive analysis of both tracheostomy and patient survival. The logistic regression will be used:

$$\log \left(\frac{p}{1-p} \right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_n x_n$$

4. Comparision and Evaluation

Since the outcome of our model is binary, we used AIC, BIC, Brier score, and area under the curve (AUC) to evaluate our models on the test datasets, which represent 30% of the data excluding the training set. AUC

can be used to compare their discrimination ability, which is the ability of the model to differentiate between people with and without the outcome. Table 4 displays the summary statistics. The mixed-effects model demonstrated significantly lower AIC and BIC values at 405 and 536, suggesting a superior fit compared to other models. The Ridge regression model exhibited the highest AUC value, suggesting enhanced predictive accuracy for binary outcomes. Brier scores were similar across models, with the Ridge model slightly better than the others, indicating predictions more closely aligned with actual outcomes. However, the notably lower AIC and BIC values for the mixed-effects model underscore the significance of including the random effect of the `center` variable.

Table 5 presents the thresholds of the four models that maximize the sum of sensitivity and specificity, respectively. All four thresholds range between 0.1 and 0.2, the specificity values are around 0.85, and the sensitivity values lie between 0.86 to 0.92.

Table 4: AIC, BIC, Brier Score and AUC

	Mixed-effects	Best Subset	Lasso	Ridge
AIC	404.5500	1693.4300	1761.620	1717.9800
BIC	535.6500	1705.6900	1773.880	1730.2400
Brier	0.0745	0.0677	0.070	0.0673
AUC	0.9177	0.9326	0.931	0.9360

Table 5: Specifity and Sensitivity at Thresholds

	threshold	specificity	sensitivity
Mixed-effects	0.1472	0.8525	0.8648
Best Subset	0.1142	0.8540	0.8941
Lasso	0.1720	0.8799	0.8814
Ridge	0.1384	0.8636	0.9110

In order to further compare best subset in a intuitive way, lasso and ridge, the calibration and the receiver operating characteristic (ROC) curve are plotted in Figure 1. Calibration assesses the agreement between observed event frequencies and predicted probabilities. It is visualized through a calibration plot, which contrasts the predicted probabilities against observed event rates, illustrating how well the predictions match actual outcomes. All three models exhibit good calibration, closely tracking the ideal 45-degree line. Notably, the lasso model’s calibration plot demonstrates the tightest adherence to this line, suggesting superior calibration accuracy.

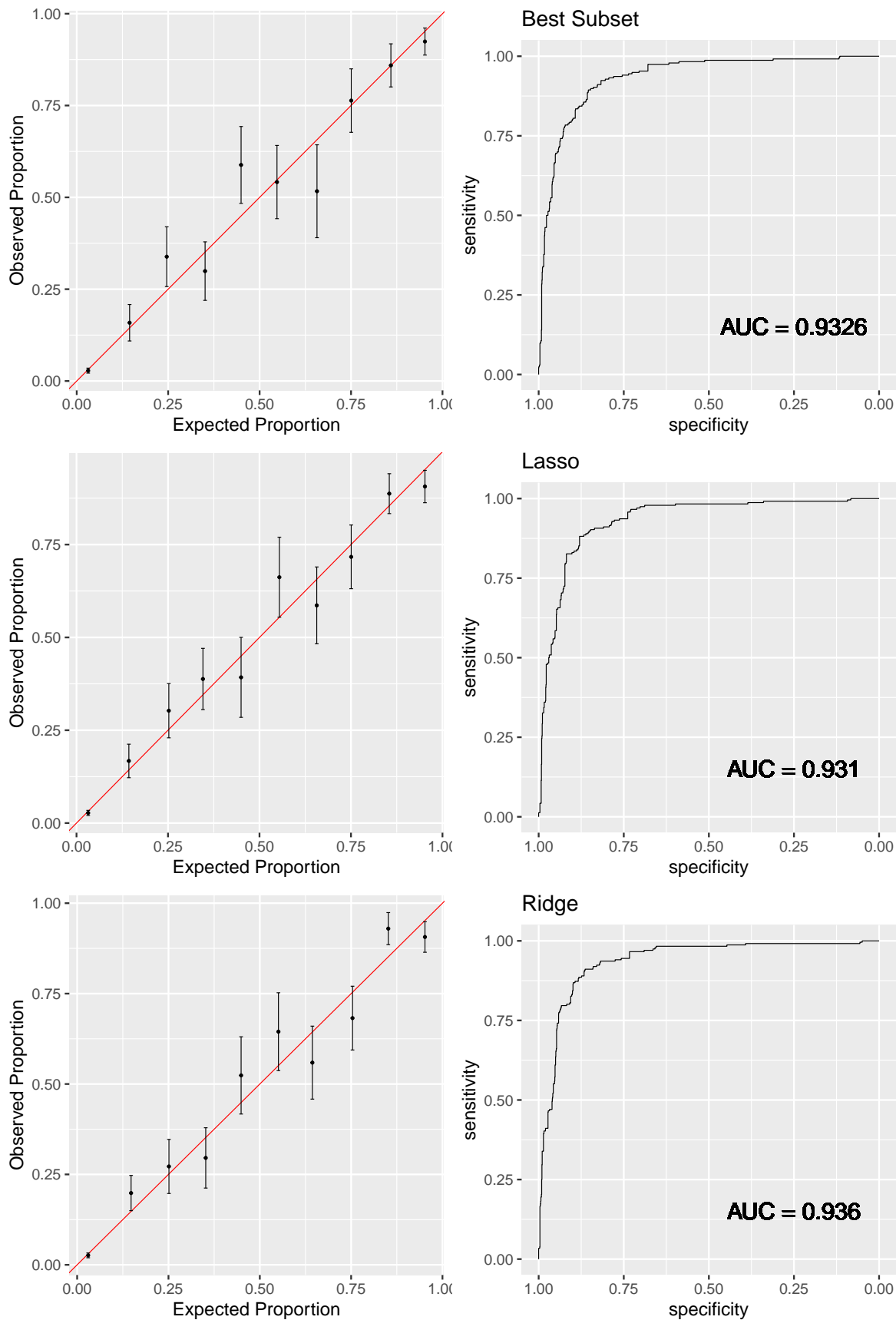


Figure 1: Calibration Plots and ROC Curves for the Six Models

5. Discussion

Table 6: Model Coefficients

	Mixed-effects	Best Subset	Lasso	Ridge
(Intercept)	-0.463	0.205	-4.701	-4.317
center2	-	-0.087	-0.347	-0.46
center3	-	-0.119	-0.791	-0.88
center4	-	-0.119	-0.172	-0.161
center5	-	-0.057	-	0.119
center7	-	-0.204	-0.869	-0.931
center12	-	0.2	1.59	1.393
center16	-	-0.222	-1.248	-1.14
center20	-	-0.214	-0.219	-1.167
center21	-	0.686	3.225	3.857
mat_ethnNot Hispanic or Latino	0.677	0.056	0.429	0.497
bw	0.002	-	-	-
ga	-0.255	-0.014	-0.022	-0.024
blength	-0.025	-0.002	-0.005	-0.011
birth_hc	0.109	0.007	0.053	0.055
del_methodCesarean section	0.272	0.013	0.054	0.151
prenat_sterYes	0.877	0.031	0.499	0.476
com_prenat_sterYes	0.405	0.035	0.298	0.284
mat_chorioYes	-0.021	-0.009	0.013	0.087
genderMale	0.055	0.008	0.004	0.053
sgaSGA	0.524	0.028	0.173	0.233
any_surfYes	-0.173	-0.013	0.007	-0.015
weight_today.36	-0.001	-	-	-
ventilation_support_level.36Non-invasive positive pressure	-0.898	-0.013	-0.211	-0.348
ventilation_support_level.36Invasive positive pressure	-0.312	0.086	0.608	0.48
inspired_oxygen.36	1.925	0.316	1.713	1.389
p_delta.36	0.028	0.001	0.012	0.015
peep_cm_h2o_modified.36	0.127	0.004	0.041	0.049
med_ph.36	-0.404	-0.03	-0.038	-0.062
weight_today.44	-	-	-	-
ventilation_support_level_modified.44Non-invasive positive pressure	-0.934	-0.144	-0.095	-0.334
ventilation_support_level_modified.44Invasive positive pressure	1.223	0.103	1.382	0.841
inspired_oxygen.44	0.57	0.067	0.621	0.913
p_delta.44	-0.01	-	0.003	0.01
peep_cm_h2o_modified.44	0.135	0.017	0.054	0.071
med_ph.44	1.406	0.17	1.126	0.938
hosp_dc_ga	0.009	0.001	0.007	0.006

In this project, four regression models are used to predict the necessity and timing of tracheostomy placement within a clinical environment, utilizing a multi-center dataset encompassing a spectrum of demographic and clinical variables. Table 6 presents the model coefficients, quantifying each variable’s impact on the likelihood of tracheostomy or mortality (denoted as Y). Here, positive coefficients indicate an elevated risk, while negative coefficients suggest a mitigating effect on the outcome.

Lower birth metrics, such as birth weight (**bw**), gestational age (**ga**) is a signal of increased risk of complications, potentially necessitating an earlier tracheostomy. These relationships are mirrored in the coefficients’ directions and magnitudes within our model. The delivery method (**del_method**), however, does not exhibit statistical significance.

Moreover, the variables representing ventilation support levels at 36 and 44 weeks were not statistically significant, whereas the fraction of inspired oxygen at 36 weeks (`inspired_oxygen.36`) was significant, contrary to its 44-week counterpart (`inspired_oxygen.44`). This variance at different time points suggests that oxygen levels are critical for determining the tracheostomy’s timing. The medications for pulmonary hypertension (`med_ph.36` and `med_ph.44`) show divergent significance levels at these time points, indicating the severity of underlying pulmonary conditions and their importance in timing the procedure.

Notably, birth weight (`bw`) and weight at 44 weeks (`weight_today.44`) are significant, while weight at 36 weeks (`weight_today.36`) and smallness for gestational age (`sga`) are not, highlighting the importance of considering weight variables in different aspects. Gender appears to have minimal impact on the outcomes. The completion of prenatal steroid courses (`prenat_ster` and `com_prenat_ster`) emerges as protective, reducing the likelihood of adverse outcomes.

Tracheostomy decisions should be comprehensive, incorporating the distinct clinical indicators underscored by our model. Key predictors—such as inspired oxygen fraction, birth metrics, pulmonary hypertension treatment, and prenatal steroid administration—form a strategic basis for clinicians to evaluate BPD severity and guide tracheostomy timing and necessity for each infant.

It is interesting that the mixed-effects model has coefficients with larger magnitudes than those obtained from the best subset, lasso, and ridge regression models. This is likely due to the intrinsic design of mixed-effects models, accounting for both fixed and random effects. The inclusion of random effects accounts for center variability, potentially magnifying the fixed effects’ coefficients to more accurately reflect the effects of individual predictors. In contrast, lasso and ridge regression incorporate regularization penalties that constrain coefficient sizes to prevent overfitting and manage multicollinearity, while the best subset selection focuses on a limited number of predictors, potentially leading to a minimization of coefficient estimates.

However, the models in this project are limited by certain assumptions required for logistic regression: the assumption of linearity, the influence of outliers, and the presence of multicollinearity. Our models do not include interaction terms to assess the linearity assumption. The residual plots seem to indicate the presence of some outliers, suggesting potential influential values. Furthermore, the ventilation support variables at 36 and 44 weeks have very high VIF values, indicating potential multicollinearity.

6. Conclusion

The exploratory data analysis and regression models used in this study offer a comprehensive understanding of the factors influencing the necessity and timing of tracheostomy in infants with severe BPD. The models highlight the significance of birth metrics, respiratory support requirements, and medication for pulmonary hypertension as pivotal indicators. Notably, the mixed-effects model, with its capacity to encapsulate both fixed and random effects, showcased larger coefficient magnitudes, underscoring the complexity and variability inherent in multi-center clinical data. However, it is crucial to recognize the limitations presented by logistic regression assumptions, which include the need for linearity, the absence of influential outliers, and multicollinearity, areas where our models require further refinement.

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