The Impact of Neurobehavior on Feeding Outcomes in Neonates with Congenital Heart Disease Analysis Report

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Log

- This is the first analysis report presented to Tom Greene:
  - Dataset used is "NNNS_Score_Data";
  - SAP used to generate report is "Group Project Statistical Analysis Plan.docx";
  - Time used for this project until now is 10 hours.

Abstract

Neurodevelopmental delay in neonates with congenital heart disease (CHD) is one of many factors contributing to their difficulty in achieving full oral feeds following neonatal cardiac surgery. Worse long-term feeding outcomes were associated with abnormalities in neonatal neurobehavior among premature infants. This project is to analyze a dataset from a retrospective, single-center cohort study. We found:

*Results from the final model for our beta regression showed that pre and post attention scores are not significantly associated with the percentage of full feeds.

*Results from our final model for our Cox regression showed pre and post attention scores are not significantly associated with the time to full oral feeds.

*Results from our sensitivity analysis give similar results to our original analyses.

Data

- Version of data: We use the NNNS_Score_Data dataset that Angela provided to us earlier this semester. There are 129 total observations;
- We excluded the columns pre- and post- habituation scores because over 70% of their observations were missing, and they were not of interest to the investigators. Although included, we decided not to analyze length of stay as it is in the causal pathway for the other variables, we are interested in.
- We excluded observations in which there was no start date for feeds and observations that did not have a completion or censoring date.

– Variable definitions:

  Outcomes are “Percentage of oral feeds at discharge” (continuous on [0,1]) and “Time to achieve full oral feed” (Obtained by calculating the number of days between start and end date with attention given to censoring).

  Explanatory variables include pre- and post- attention scores (continuous variables). Other variables controlled for in the analysis are sex (male or female), genetic syndrome (Y/N), age at surgery (days), prematurity (Y/N), cardiac anatomy (four types), length of intubation (days), extubation failure (Y/N), and gastrointestinal complications (Y/N).

– Cohort construction:

Cohort	Size
Total number of observations	129
Excluded observations that do not have starting date	121
Excluded observations that also did not have either ending date or censoring date	118

Research Objectives

The research objectives for this analysis are to:

- Determine if lower pre- or post-op attention scores are associated with a lower percentage of oral feeds at discharge after adjusting for sex, genetic syndrome, age at surgery, prematurity, cardiac anatomy, length of intubation, extubation failure (Y/N), and gastrointestinal complications.
- Determine if lower pre- or post-op attention scores are associated with a longer time to achieve full oral feeds after cardiac surgery after adjusting for sex, genetic syndrome, age at surgery, prematurity, cardiac anatomy, length of intubation, extubation failure (Y/N), and gastrointestinal complications.

Statistical Methods

All of our calculations and modeling was done in R.

Before approaching the research questions, we had to handle the missing data. In order to do this, we used multiple imputations with default parameters for the data. While we considered looking for correlated NNNS scores to predict the pre- and post- attention scores, we decided to use all variables in the imputation. We then computed the pooled results of the imputations.

We included a sensitivity analysis that uses the lowest pre- and post- attention scores for the missing pre- and post- attention scores. After filling the missing pre and post attention scores with their minimum, we used multiple imputation to impute percentage of oral feeds at discharge.

To determine if lower pre- and post- attention scores are associated with percentage of oral feeds at discharge, we used zero-inflated beta regression using the gmlss package. We handled the 1s in the date by using a transform (y*(n-1) + 0.5) / n for all values that were not 0. To determine if number of days it takes to obtain a full oral feed is related to pre and post attention scores, we used a Cox regression.

Result

Tables and Figures

Table 1 Descriptive Summary.

Variable	Levels	Summary (N=118)
Sex	Male	70 (59.3%)
Genetic Syndrome or Chromosomal Abnormality	Yes	21 (17.8%)
Age (Surgery days)	Mean (SD)	8.8 (7.8)
	Median (IQR)	7.0 (5.0, 10.0)
	Range	(0.0, 70.0)
Premature	Yes	104 (88.1%)
Cardiac Anatomy	Single ventricle w/ arch obstruction	28 (23.7%)
	Single ventricle w/o arch obstruction	10 (8.5%)
	Two ventricle w/ arch obstruction	39 (33.1%)
	Two ventricle w/o arch obstruction	41 (34.7%)
Length of intubation days	Mean (SD)	5.0 (2.7)
	Median (IQR)	4.9 (3.1, 6.1)
	Range	(0.4, 19.0)
Extubation failure	Yes	11 (9.3%)
GI Complication	Yes	10 (8.5%)
Pre-Operation NNNS attention score	Mean (SD)	3.4 (1.0)
	Median (IQR)	3.4 (2.9, 4.0)
	Range	(0.5, 5.5)
Post Operation NNS attention score	Mean (SD)	4.4 (1.0)
	Median (IQR)	4.4 (3.9, 5.0)
	Range	(2.0, 7.1)

Missing values: Pre-Operation NNNS attention score=58, Post Operation NNS attention score=37.

Figure 1

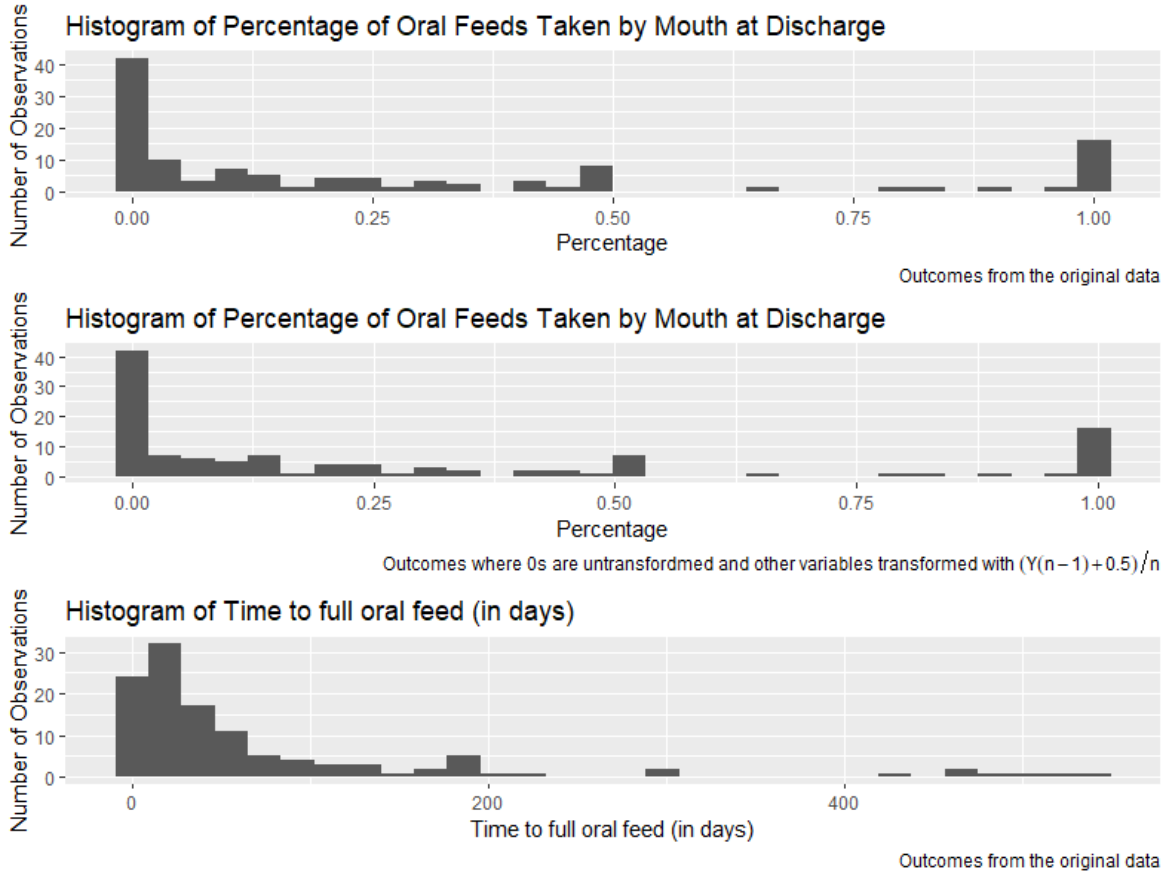

Figure 2

Table 2:Odds Ratios from the Regression. Association between Percentage of Oral Feeds and Attention scores

	Odds Ratio	2.5 %	97.5 %	p.value
Intercept	0.898	0.263	3.064	0.86
Sex, ref = male	0.872	0.262	2.901	0.819
Genetic syndrome - Yes	0.917	0.275	3.052	0.885
Age at surgery (days)	0.927	0.269	3.199	0.902
Premature - Yes	0.881	0.257	3.015	0.836
Cardiac Anatomy	0.914	0.258	3.23	0.885
Length of Intubation (days)	0.945	0.273	3.278	0.928
Extubation Failure - Yes	0.871	0.3	2.528	0.795
GI Complication - Yes	0.928	0.267	3.23	0.905
Pre-Op Attn Score	0.98	0.196	4.907	0.979
Post-Op Attn Score	0.982	0.303	3.185	0.975

Table 3: Results from Cox Regression. Association between Time to Full Feed and Pre Post Attention Scores

	Hazard Ratio	2.5 %	97.5 %	p.value
Sex, ref = male	2.689	0.704	10.274	0.148
Genetic syndrome - Yes	1.651	0.407	6.696	0.482
Age at surgery (days)	0.777	0.597	1.01	0.06
Premature - Yes	1.036	0.186	5.76	0.968
Cardiac Anatomy	1.205	0.605	2.401	0.594
Length of Intubation (days)	1.121	0.949	1.325	0.179
Extubation Failure - Yes	1.65	0.355	7.674	0.522
GI Complication - Yes	2.079	0.382	11.321	0.397
Pre-Op Attn Score	0.602	0.267	1.356	0.22
Post-Op Attn Score	1.807	0.771	4.234	0.173

Table 4: Results from Beta and Cox Regression of Percentage of Oral Feeds and Time to Full Feed respectively onto Pre-Attention Scores.

	Odds Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
Intercept	1.009(0.255,3.997)	0.99	-	-
Sex, ref = male	0.849(0.354,2.037)	0.704	0.81(0.642,1.022)	0.075
Genetic syndrome - Yes	0.848(0.358,2.006)	0.698	1.504(0.827,2.734)	0.181
Age at surgery (days)	0.855(0.357,2.049)	0.716	1.368(0.304,6.156)	0.683
Premature - Yes	0.985(0.257,3.775)	0.982	1.013(0.325,3.154)	0.982
Cardiac Anatomy	0.986(0.262,3.708)	0.983	2.78(0.56,13.797)	0.211
Length of Intubation (days)	1.022(0.261,4.004)	0.975	1.105(0.936,1.305)	0.239
Extubation Failure - Yes	0.851(0.358,2.024)	0.707	0.61(0.261,1.425)	0.252
GI Complication - Yes	0.979(0.252,3.806)	0.975	1.026(0.177,5.958)	0.977
Pre-Op Attn Score	0.852(0.351,2.069)	0.713	3.252(0.893,11.844)	0.074

Table 5: Results from Beta and Cox Regression of Percentage of Oral Feeds and Time to Full Feed respectively onto Post Attention Scores.

	Odds Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
Intercept	1.091(0.166,7.188)	0.924	-	-
Sex, ref = male	0.845(0.351,2.037)	0.699	0.796(0.635,0.997)	0.047
Genetic syndrome - Yes	0.836(0.349,2.002)	0.678	1.279(0.688,2.38)	0.437
Age at surgery (days)	0.833(0.355,1.954)	0.665	2.684(0.733,9.834)	0.136
Premature - Yes	0.992(0.229,4.3)	0.992	1.434(0.397,5.176)	0.582
Cardiac Anatomy	1.073(0.212,5.43)	0.931	2.167(0.434,10.83)	0.346
Length of Intubation (days)	1.001(0.227,4.421)	0.999	1.086(0.942,1.252)	0.256
Extubation Failure - Yes	0.824(0.346,1.962)	0.651	1.756(0.77,4.005)	0.18
GI Complication - Yes	0.938(0.209,4.208)	0.932	1.387(0.277,6.958)	0.691
Post-Op Attn Score	0.835(0.345,2.019)	0.678	2.086(0.664,6.553)	0.208

Table 6: Correlation matrix of the NNNS score variables and attention scores

	Pre-Op Attention Score		Post Op Attention Scores	
	Correlation	**p.value**	**Correlation**	**p.value**
Handling	0.148	0.259	-0.161	0.153
Quality of Movement	-0.104	0.431	0.099	0.381
Regulation	0.133	0.312	0.058	0.609
Non-Optimal Reflexes	-0.463	**0**	0.118	0.295
Stress	-0.221	0.093	-0.02	0.862
Arousal	-0.071	0.588	0.166	0.138
Hypertonic	0.088	0.502	0.013	0.905
Hypotonic	-0.324	**0.012**	-0.137	0.222
Asymmetry	-0.047	0.721	0.165	0.141
Excitability	0.094	0.476	0.03	0.787
Lethargy	-0.703	**0**	-0.642	**0**

Table 7: Sensitivity Analysis - Odds Ratios from the Regression of Percentage of Oral Feeds onto Attention scores

	Odds Ratio	2.5 %	97.5 %	p.value
Intercept	0.962	0.316	2.928	0.943
Sex, ref = male	0.931	0.294	2.948	0.9
Genetic syndrome - Yes	0.933	0.297	2.924	0.902
Age at surgery (days)	0.964	0.308	3.015	0.948
Premature - Yes	0.951	0.308	2.934	0.928
Cardiac Anatomy	0.914	0.292	2.867	0.875
Length of Intubation (days)	0.94	0.295	2.997	0.915
Extubation Failure - Yes	0.868	0.312	2.414	0.78
GI Complication - Yes	0.952	0.307	2.946	0.93
Pre-Op Attn Score	0.921	0.33	2.571	0.872
Post-Op Attn Score	0.942	0.304	2.912	0.915

Table 8: Sensitivity Results from Cox Regression of Time to Full Feed onto Pre and Post Attention Scores

	Hazard Ratio	2.5 %	97.5 %	p.value
Sex, ref = male	2.522	0.814	7.813	0.109
Genetic syndrome - Yes	0.961	0.313	2.945	0.944
Age at surgery (days)	0.81	0.649	1.012	0.064
Premature - Yes	1.434	0.27	7.62	0.672
Cardiac Anatomy	1.633	0.913	2.92	0.098
Length of Intubation (days)	1.085	0.938	1.254	0.271
Extubation Failure - Yes	2.319	0.629	8.555	0.207
GI Complication - Yes	3.167	0.693	14.468	0.137
Pre-Op Attn Score	1.134	0.802	1.605	0.477
Post-Op Attn Score	0.979	0.569	1.687	0.94

Table 9: Sensitivity Analysis: Results from Beta and Cox Regression of Percentage of Oral Feeds and Time to Full Feed respectively onto Pre-Attention Scores.

	Odds Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
Intercept	1.02(0.277,3.765)	0.975	-	-
Sex, ref = male	0.858(0.362,2.032)	0.718	0.811(0.651,1.011)	0.062
Genetic syndrome - Yes	0.857(0.367,2.002)	0.713	1.618(0.957,2.734)	0.073
Age at surgery (days)	0.85(0.355,2.035)	0.705	2.289(0.651,8.039)	0.197
Premature - Yes	1.026(0.277,3.807)	0.968	0.974(0.337,2.818)	0.961
Cardiac Anatomy	0.987(0.258,3.779)	0.984	3.211(0.734,14.037)	0.121
Length of Intubation (days)	1.013(0.277,3.703)	0.984	1.084(0.938,1.252)	0.273
Extubation Failure - Yes	0.857(0.361,2.035)	0.717	1.131(0.806,1.586)	0.476
GI Complication - Yes	1.004(0.267,3.769)	0.995	1.444(0.276,7.559)	0.664
Pre-Op Attn Score	0.855(0.366,1.998)	0.709	2.505(0.82,7.653)	0.107

Table 9: Sensitivity Analysis: Results from Beta and Cox Regression of Percentage of Oral Feeds and Time to Full Feed respectively onto Post-Attention Scores.

	Odds Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
Intercept	1.071(0.242,4.735)	0.926	-	-
Sex, ref = male	0.836(0.36,1.939)	0.666	0.823(0.665,1.018)	0.072
Genetic syndrome - Yes	0.834(0.365,1.905)	0.657	1.589(0.901,2.802)	0.11
Age at surgery (days)	0.827(0.354,1.934)	0.651	2.216(0.614,7.993)	0.224
Premature - Yes	1.073(0.241,4.789)	0.924	0.952(0.307,2.949)	0.932
Cardiac Anatomy	1.034(0.224,4.779)	0.964	2.957(0.661,13.218)	0.156
Length of Intubation (days)	1.065(0.24,4.719)	0.932	1.068(0.93,1.227)	0.352
Extubation Failure - Yes	0.833(0.358,1.937)	0.661	1.022(0.599,1.744)	0.936
GI Complication - Yes	1.05(0.23,4.788)	0.948	1.374(0.263,7.172)	0.706
Post-Op Attn Score	0.832(0.364,1.9)	0.652	2.589(0.844,7.941)	0.096

Text

Results from the final model for our beta regression showed that pre and post attention scores are not significantly associated with the percentage of full feeds.

Results from our final model for our Cox regression showed pre and post attention scores are not significantly associated with the time to full oral feeds.

Results from our sensitivity analysis give similar results to our original analyses.

Discussion

First, results from the final model for our beta regression showed that pre and post attention scores are not significantly associated with the percentage of full feeds. We found this curious because we thought that something would be significant. To double check this, we did a beta regression with the original data. This showed again that nothing was significant. Because the standard errors are different among imputations, we expect to see higher p-values with the imputed data.

Moreover, we performed the beta regression to see the association between pre attention score and percentage of oral feed at discharge excluding the post attention score from the model. We found that they are not associated. We also applied the same model between post attention score and percentage of oral feed at discharge but this time excluding the pre attention score. We have found post attention score and percentage of oral feed at discharge are almost significantly associated.

Second, results from our final model for our Cox regression showed pre and post attention scores are not significantly associated with the time to full oral feeds. Again, we were worried about not finding a significant result. However, through conducting our sensitivity analysis, we saw a similar result again that there is not significant predictor for the time it takes to obtain a full oral feed.

Our sensitivity analysis confirmed our results for both the beta regression and survival analysis.

Additional Information for Project PI

Guidelines for Authorship

In general, authorship is merited and expected for PHR/SDBC statisticians and collaborators. Exceptions may be made if the number of authors is limited by the journal, but please discuss with the PHR/SDBD collaborators. The criteria for authorship by the International Committee of Medical Journal Editors can be found online at: https://medicine.utah.edu/ccts/sdbc/publish.php.

PHR/SDBC Policy requires manuscripts, posters and abstracts be made available to PHR/SDBC statisticians and collaborators with reasonable time (1 week+ for papers) prior to submission.

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