CRC Project Protocol:
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Title of Project: Cardiac Surgical Outcomes in Premature Infants with Congenital Heart Disease

Research Aims:
To assess the hospital mortality after cardiac surgery in neonates born at ≤ 37 weeks of gestation compared to those born at 38-42 weeks of gestation in an institution with a dedicated neonatal cardiac program and to investigate the risk factors for mortality in these infants.

Scientific Abstract:
Prematurity and low-birth weight are well known risk factors for poor outcomes in neonates undergoing cardiac surgery[2-4]. As one of the largest pediatric cardiology centers in the country, the Morgan Stanley Children's Hospital of New York Presbyterian (MSCHONY) cares for a large number of infants with congenital heart disease who undergo cardiac surgery early on in the neonatal period. A recent study done by Kalfa and associates looking at outcomes of low birth weight patients (<2.5kg) found that a lower gestational age at birth was an independent risk factor for hospital mortality and may actually be more important than birth weight in terms of increasing mortality in infants[4]. This is a single-center retrospective analysis to assess the hospital mortality after cardiac surgery in neonates born at ≤ 37 weeks of gestation compared to those born at >/= 37 weeks of gestation in an institution with a dedicated neonatal cardiac program with the goal of determining the risk factors for mortality in these infants. The information gained from the review can potentially have significant benefit to the care of infants with congenital heart disease in the future if we can better understand the factors related to morbidity and mortality for these patients.

STUDY DESCRIPTION
Study Purpose & Rationale:
Congenital heart defects affect nearly 40,000 infants in the United States each year and out of these 40,000, 25% have critical CHD requiring surgical intervention within the first year of life[1]. Despite advances in the perinatal and surgical management, which have resulted in improved outcomes, there continues to be high rate of mortality and significant morbidity experienced by survivors. Thus, there is a need to examine potentially modifiable risk factors for poor outcomes.

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Thus, the primary goal of this study is to assess the hospital mortality after cardiac surgery in neonates born at ≤ 37 weeks of gestation compared to those born at 38-42 weeks of gestation in an institution with a dedicated neonatal cardiac program and to investigate the risk factors for mortality in these infants.

Study Design and Statistical Procedures:

This is a retrospective single-center- cohort- study of all neonates who were admitted to the neonatal intensive care of Morgan Stanley Children's Hospital of New York Presbyterian with congenital heart disease and who underwent cardiac surgery in the neonatal period from January 1, 2006- December 31, 2015.

Study Site:

- Level 4 Neonatal Intensive Care Unit with ~1200 admissions and ~110 cardiac surgeries annually. The NICU has a dedicated neonatal cardiac program where infants are cared for from admission to discharge by a dedicated team of medical and nursing staff from neonatal intensive care, pediatric cardiology, and pediatric cardiac surgery

Eligible Subjects:

- Infants who underwent cardiac surgery at The Morgan Stanley Children's Hospital from January 1, 2006 – December 31, 2015
- Will exclude infants whose gestational age could not be determined, if initial cardiac surgical procedures was performed at another institution, fatal genetic syndromes (ex: trisomy 13) or additional major malformations if life support was withdrawn before cardiac intervention.

Sample Size:

- ~1,100 neonates who underwent cardiac surgery within the neonatal period at Morgan Stanley Children's Hospital

Explanatory Variables:

- Gestational age at birth
- Demographic characteristics such as gender, birth weight, weight at surgery, chronologic age at surgery
- Clinical characteristics such as prenatal diagnosis, associated congenital anomalies (anatomic or chromosomal), single ventricle physiology, surgical STS-EACTS risk category (representative of operative difficulty).

Primary Outcome:

- In-hospital mortality

Secondary Outcomes:

- Post-op length of stay
- Post-op complications

Statistical Analysis:

- Survival analysis will be performed using Kaplan- Meir survival curves
- Outcomes will be assessed using univariable and multivariable analyses.
- Univariable analyses will include Chi-squared tests to assess the effects of categorical variables on categorical outcomes, and t-tests to assess the effects of continuous variables on categorical outcomes.
- In multivariable analyses, logistic regression will be used to assess associations between potential risk factors for mortality and composite morbidity with preterm birth.

<u>Potential Benefits</u>

A retrospective chart review will have no immediate benefit to the patients. However, the information gained from the review can potentially have significant benefit to the care of infants with congenital heart disease in the future if we can better understand the factors related to morbidity and mortality for these patients

Confidentiality

All the data will be de-identified and given a unique and given a unique study number to maintain confidentiality.

Potential Risk

As this study consists of a retrospective chart review, there is no risk to the patient. The only potential risk is to the confidentiality of the patient, which will be minimized by the above mentioned fashion.

References:

1. Congenital heart defects. Centers or Disease Control and Prevention. Available at http://www.cdc.gov/ncbddd/heartdefects/data.html Accessed March 19, 2016

2. Costello JM et al. Gestational Age at Birth and Outcomes after Cardiac Surgery: An analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Circulation* 2014, 129:2511-2517

3. Costello JM, Polito A, Brown DW, McElrath TF, Graham DA, Thiagarajan RR, et al. Birth before 39 weeks gestation is associated with worse outcomes in neonates with heart disease. J *Pediatrics.* 2010: 126; 137:653-9

3. Curzon CL, Milford-Beland S, Li JS, O'Brien SM, Jacobs ML, et al. Cardiac Surgery in infants with low birth weight is assoicatd with increased mortality: analysis of of the Society of Thoracic Surgeons Congenital Heart Database, *J Thorac Cardiovascular Surgery.* 2008 135:546-51

4. Kalfa D, Krishnamurthy G, Duchon J, Najjar M, Levasseur S. Chai P, et al. Outcomes of cardiac surgery in patients less than 2.5kg: Affect of patient-dependent and –independent variables. *Journal of Thoracic Cardiovascular Surgery*. 2014; 148: 2499-2506.