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CRC Research Course

One-Year Growth for Tetralogy of Fallot Patients with Neonatal Surgical Repair versus Those Repaired Later in First Year of Life.

Study Purpose and Rationale:

Tetralogy of Fallot (TOF), originally described by Etienne-Louis Arthur Fallot in 1888 as "la maladie bleue" (blue malady), is a common congenital heart lesion, representing approximately 10% of congenital cardiac malformations. It is one of the most common causes of cyanotic heart disease beyond the neonatal age[i]. There are four main components of the tetralogy: ventricular septal defect (VSD), right ventricular outflow tract obstruction (RVOTO), an overriding aorta, and right ventricular hypertrophy (RVH). There are several subtypes of TOF including, associated absent pulmonary valve syndrome, common atrioventricular canal, pulmonary atresia, and the most common, pulmonary stenosis. There are also frequent anatomical associations with TOF including right aortic arch (25%), left anterior descending (LAD) coronary artery off the right coronary artery (RCA) (5%), branch pulmonary artery anomalies (30% of infants presenting in first year of life), major aortopulmonary collarterals (<5%), foramen ovale, and atrial septal defects (10%)[ii]. Surgical intervention in necessary for long-term survival in these patients; without it twenty-five percent of patients with severe obstruction will die within the first year.

The evolution of surgical interventions began with the Blalock-Taussig shunt, first performed in 1944, and has progressed to the intracardiac repair in 1954, the transannular patch in the 1970s, and the pulmonary valve-sparing repair since the 1990s. While patients were initially repaired between ages 3 to 5 years old, over time studies showed improved mortality with those patients that underwent complete repair during the first year of life. Current recommendations are that patients undergo complete repair by age 6 months, and no later that 12 months, for those patients that are not ductal dependent, and asymptomatic[iii].

Keeping with these recommendations, there is still debate about the exact timing of intervention. Additionally the optimal type of initial surgical intervention, (ie. Two-stage repair with shunt prior to complete repair, versus an initial complete repair) remains controversial[iv]. There is also variation of the clinical presentation, therefore some patients are repaired within the first few weeks of life, and some are repaired later during the first year of life. Patients with severe cyanosis associated with pulmonary atresia or severe pulmonary stenosis require urgent surgical repair after birth, but the controversy persists for other patients with TOF and pulmonary stenosis, and less severe RVOTO. The rationale behind early surgical intervention is to relieve pressure from the right ventricle (RV) in an attempt to prevent hypertrophy, to improve cyanosis and secondary polycythemia, to prevent long-standing structural changes of the heart, and to improve oxygen delivery earlier in development. The downsides to neonatal repair are small size, potentially changing hemodynamics and anatomy, as well as, concerns for worse side effects of bypass on the neonatal brain[v]. Conversely, later surgical repair has been associated with less post-operative complications given the larger size, higher likelihood of complete one stage repair, and more stable physiology after the first month of life[vi-vii]. The downsides of later surgical intervention, however, are longer time with increased work for the right ventricle,

which may lead to right ventricular hypertrophy, in addition to persistent hypoxemia, both of which can lead to ventricular dysfunction and arrhythmias[viii].

One study by Van Arsdell et al, attempted to answer this question during a policy transition period at Hospital for Sick Children in Toronto from 1993 to 1998, in which the standard of care changed at this institution from a two-step repair with a palliative shunt to correction with a single complete repair. This study found that overall mortality fell from 2.6% to 0% after the change, although primary repair in infants less than 3 months of age was associated with a longer ICU stay. Given that those single repairs were usually done between ages 3 to 6 months, they concluded that the optimal time for surgical repair was between 3 to 6 months of age[ix-x]. The limitations of this study are that it was at a single institution, therefore it is difficult to extrapolate findings to all institutions, and single repairs are now technically feasible in the neonatal period, which may change the concluded optimal timing. Despite the results of this study, there continues to be controversy. The decision for timing of surgical intervention is a multi-factorial decision made by the primary cardiologist, in conjunction with the surgeons and parent's input. Ultimately the type of surgical repair, ie complete repair versus two-stage repair, is determined by the surgeon with consideration for the technical feasibility of the procedure, size of the patient, and personal experience and skill level.

In this study we aim to provide more information about the difference in growth outcomes between those patients with Tetralogy of Fallot that undergo surgical intervention in the neonatal period versus those that undergo intervention later in the first year of life. We will look specifically at the change in weight and height over one year and determine if there is a difference between the two groups. Several studies have shown the connection between growth and developmental outcomes in children[xi]. Belfort et al showed that greater weight gain in preterm infants to term and after term were associated with better neurodevelopmental outcomes[xii]. Given this connection, this study may provide information to pediatric cardiologists and surgeons about the impact of timing of surgical intervention on growth and neurodevelopment in patients with Tetralogy of Fallot. To our knowledge there have been no studies looking specifically at growth outcomes in patients with TOF.

Study Design and Statistical Procedures:

Aim I: To investigate the impact of timing of surgical intervention on one-year growth outcomes for infants born with TOF. Hypothesis: Those patients who undergo early surgical intervention will have improved growth outcomes compared to those patients who undergo surgical intervention later in the first year of life.

Study design:

This is a retrospective cohort study. Data will be collected retrospectively from medical records of operative reports and hospital stay in the NICU and post-operatively. This database will include all infants with congenital cardiac lesions admitted to the neonatal intensive care unit (NICU) at the Children's Hospital of New York between 2004 and 2011. Growth data including weight, length, and head circumference will be collected throughout the first year of life. For those patients admitted to our NICU and surgically repaired at our hospital but who were followed post-operatively elsewhere, the primary cardiologist will be contacted to obtain growth data at one-year.

Data will also be collected to provide information about the about the severity of illness and perioperative complications, including respiratory status (ie. need for NC, CPAP, or intubation), the need and duration of prostaglandin, the need and duration of pressor support, and the need and duration of ECMO support. Possible covariate data will also be collected including genetic syndromes, other anatomic diagnoses, need for other procedures or surgical repairs, means of feeding, type of formula, number of hospitalizations, and other complications during their hospital stay. Surgical operative reports and echocardiogram reports will be reviewed to provide a detailed anatomic description of the lesion.

In this study we will focus on the subset of patients with TOF that are not ductal dependent, including patients with TOF and pulmonary stenosis, as well as those with double outlet right ventricle (DORV) and pulmonary stenosis and Tet-like physiology. We have included the latter congenital cardiac defect, given the similar physiology and similar surgical repair required. A blinded pediatric cardiologist will review a select amount of information, including type of lesion, neonatal saturation, ductal dependence, gestational age and size, in order to determine if the subject qualifies for our propensity group, which includes patients that arguably could have neonatal surgery or wait until 4-6 months of age for repair. Only these subjects will be included in our statistical analysis. We will compare weight, and height at one year of life (+/- 2 months) to determine if there is a different between the early versus late surgical repair group, and then carry out a statistical analysis to see if that difference is statistically significant.

Statistical Analysis:

An unpaired t-test is the most appropriate statistical analysis method for this study given that our outcome measure (weight) is a continuous measure. The likely range of growth over one-year is from 3 to 7 kilograms. This range has a standard deviation of 1 kilogram. Therefore, in order to power our study to an 80% confidence, testing at $p<0.05$ and to detect an effect equal to one standard deviation (ie. 1 kg difference between the early surgical repair group and the late surgical repair group), we will need 17 subjects in the early surgical intervention group and 17 subjects in the later surgical intervention group. In order to detect a statistically significant effect of 0.5kg or one half standard deviation, each group would need to have 56 subjects.

Study procedures:

This study will consist of retrospective review of subject's medical record including medical and birth history, diagnosis, laboratory information, prenatal history including fetal echocardiogram, and the other data listed above. This is purely a retrospective chart review, and includes only information that were part of the standard of care for the particular patients, and will not require any addition data, studies, or tests to be obtained.

Study Drugs of Devices: N/A

Study Questionnaires: N/A

Study subjects:

The study population includes all patients admitted to the neonatal intensive care unit at the Morgan Stanley Children's Hospital of New York between 2004 and 2011 with the diagnosis of TOF or DORV/PS with tet-like physiology, as determined by postnatal echocardiogram. This study population was selected to include both patients born to or transferred to our NICU. This population also includes those patients that were surgically repaired while admitted to the NICU, as well as, those that were discharged from the NICU and who later returned for surgical repair to our institution. Our study will focus those patients for whom we were able to obtain one-year weight and height data. This population also excludes those patients that were surgically repaired passed the first year of life.
Given the high acuity of this institution, this population allows for an appropriate sample size for this study. These results will be generalizable with the caveat that this is data from a single institution; therefore, the outcomes are influenced by the surgical decisions and skills of a select group of pediatric cardiologists and pediatric cardiac surgeons[xiii].

Recruitment:

This is a retrospective chart and medical information review; therefore subject will not be recruited actively.

Confidentiality of Study Data:

Patient confidentiality will be maintained during data collection and analysis but assigning each patient a unique study ID number. All identifiers will be removed from files. A separate file will link the patient identifier to the study number. Access to data will be restricted to investigators only and all electronic data will be password protected.

Potential Risks:

Given that this study consists of a review of medical information, there are no physical risks to the subjects. Subjects will not be contacted directly. The only conceivable risk would be a loss of confidentiality during data collection, but subject confidentiality will be protected by the measures mentioned above.

Potential Benefits:

During this retrospective collection of data, there will be no immediate benefit to the subjects involved. It is our goal, however, to provide valuable information regarding timing of surgical intervention and growth outcomes for patients with TOF that may influence clinical decision making in the future, in order to improve future growth and therefore neurodevelopmental outcomes for this population.

Alternatives:

There are no alternatives to disclose as there are no therapeutic interventions being done in this study.

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