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Study Title: Echocardiographic Measures of Right Ventricular Systolic Function after Pediatric Heart Transplant

A. Study Purpose and Rationale

Heart transplant (HT) is an increasingly common therapy in children with heart failure. Echocardiography is a non-invasive widely available imaging modality used to assess children in the post-transplant period. The utility of echocardiography has increased in recent years with the development of pulsed-wave tissue doppler imaging (PW-TDI) and two-dimensional speckle tracking echocardiography (STE).[1] These imaging parameters been shown to be superior to conventional echo measures at detecting ventricular dysfunction.[2] Right ventricular (RV) dysfunction has been shown to be a major predictor of increased mortality in heart transplant patients.[3,4]

Since the base of the RV is one of its most easily visualized portions, quantitative assessments of its movements are used to extrapolate as to the global function of the RV. PW-TDI and STE measurements such as tricuspid annular plane systolic excursion (TAPSE) and systolic excursion velocity (S') and global longitudinal strain (GLS) provide a reproducible measurement of RV systolic function.

Several studies have been performed to assess the utility of PW-TDI and STE the detection of ventricular dysfunction on pediatric HT patients. Mahle et al.[1] performed a study using PW-TDI in 13 patients post-transplant and found that both systolic and diastolic velocities were reduced after transplant. The velocities improved in the initial 6 months following transplant. In a later study, Lunze et al.[5] performed serial echocariography on 44 pediatric HT patients using age-based normative values for systolic (*S′*), early-diastolic (*E′*), and late-diastolic (*A′*) velocities obtained using pulsed-wave tissue Doppler imaging. These authors were able to detect right ventricle (RV) systolic dysfunction that remained abnormal for 1-year post transplant. Buddhe et al.[6] performed a study on 50 pediatric HT patients that utilized STE to measure global longitudinal peak systolic strain of the left ventricle. This measurement had a weak correlation between pulmonary capillary wedge pressure (PCWP) obtained via cardiac catheterization ($r = 0.33$; $P = .02$). This correlation was stronger than traditional echocardiography parameters. Palomero et. al[7] performed a serial echocardiograms on 31 patients in the post-transplant period and detected initial ventricular dysfunction and then normalization after one year. This study also offered normal strain values that may be used for comparison.

The purpose of this study is to use STE and PW-TDI to better characterize ventricular dysfunction in the post-transplant period and correlate this dysfunction with clinical outcomes. With this increased understanding we will utilize this method as both a prognostic indicator and for the development of a non-invasive rejection surveillance protocol. Unlike previous studies, this study will include a larger sample size, and additional catheterization measures that correspond to serially performed echocardiograms.

B. Study Design and Statistical Analysis

This will be a single center retrospective study assessing echocardiographic measures of RV function serially performed following heart transplant. The first measurements were taken 1-13 days following transplant and then performed at 1, 3, 6, 9, and 12 months following transplant. These echo parameters will be correlated with catheterization pressures taken at corresponding time points. Outcomes such as mortality and graft rejection will be correlated with echo findings as well.

The imaging parameters will be transformed into age-based z scores using validated pediatric normal values.[8] The pearson correlation coefficient will be used to quantify the extent of correlation between the imaging and catheterization data. Power analysis determines that for 145 subjects the smallest correlation that can be statistically significant is $r > 0.23$.[9]

C. Study Procedure.

Echocardiographic assessment:

All transthoracic echocardiograms were acquired using the Phillips iE33 (Philips Healthcare, Andover, Massachusetts, United States of America) ultrasound machines. TAPSE was determined using the two-dimensional method where the distance from the tricuspid valve lateral annulus to the skin-transducer interface was measured at end-diastole and end-systole, with the distance expressed in centimeters. S' was similarly obtained from the pulsed tissue Doppler image of the tricuspid annulus as the peak systolic velocity in meters/second. For GLS 2D strain measurements are based on speckle-tracking imaging. The amount of deformation (positive or negative strain) is expressed in %.

Cardiac Catheterization:

Post-transplant cardiac catheterization data was obtained at 1-13 days post-transplant and 1,3,6,9 and 12 months following transplant.

D. Study Subjects

The study subjects are pediatric patients and young adults who underwent HT at Columbia University Medical Center, Morgan Stanley Children's Hospital of NewYorkPresbyterian between January 1, 2009 and December 31, 2015. Subjects will be excluded if there was lack of adequate echocardiographic data for analysis. There were 145 subjects that underwent transplant during the study period and had adequate echocardiographic data for analysis.

E. Recruitment of Subjects

All pediatric patients and young adults who underwent HT at Columbia University Medical Center, Morgan Stanley Children's Hospital of NewYorkPresbyterian between January 1, 2009 and December 31, 2015 were recruited for the study.

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