



Trawick Pediatric Cardiology Research Fund – Supporting Single Ventricle Research

Research Progress Report – April 26, 2021

The Trawick Pediatric Cardiology Research Fund has been directed to support three main areas:

1. Support for completion and dissemination of research in progress
2. Support for ongoing research or research at the proposal stage
3. Support for studies investigating novel concepts and techniques

Completion and Dissemination of Research in Progress

While the COVID-19 pandemic has altered many clinical practice patterns and research opportunities, work has successfully proceeded in all of these areas. Specifically, funds were first directed towards the completion and presentation of the paper “A Randomized, Controlled Pharmacokinetic and Pharmacodynamics Trial of Ambrisentan After Fontan Surgery.” This research demonstrated that the endothelin receptor antagonist Ambrisentan had an acceptable safety profile and favorable hemodynamic effects in Fontan patients. This may translate to clinical utility given the known endothelial dysfunction in Fontan patients limiting the effectiveness of medications that rely on the Nitric Oxide pathway.

Results from a new clinical research study were recently accepted to the American Society of Echocardiography as a research abstract, with Dr. Mariah Cicioni (a Duke Pediatrics resident planning a career in cardiology) as first author. This abstract will be presented in poster format during the Scientific Sessions, which will be held virtually between June 18 and 21. This research consisted of a retrospective review of the Duke Cardiac MRI (CMR) experience with late-gadolinium enhancement (LGE) imaging of Fontan patients to detect intracardiac thrombus. Compared to the existing echocardiographic literature, Fontan patients imaged by LGE-CMR have far fewer intracardiac thrombi detected, which leads to questions of which imaging modality is best used for screening, and what modality best used in the presence of symptoms. Following abstract presentation, this research will be converted to manuscript form and submitted for publication.

Ongoing Research

Ongoing research to be supported includes work by incoming fellow (current Duke resident) Dr. Meredith Sooy-Mossey investigating the effects of racial and educational isolation on mortality, hospital length of stay, and complications in a large, multi-institutional cohort of single ventricle patients. Preliminary results are planned to be submitted as an abstract to the American Heart



Association meeting in the fall of 2021, and it is expected that this research will continue to progress during Dr. Sooy-Mossey's fellowship.

Other ongoing research extends the CMR Fontan cohort into an investigation of the impact of ideal vs. measured body mass on cardiac measurements, function, and outcomes of single ventricle patients. This builds upon successful similar work demonstrating that use of ideal body mass may alter timing of pulmonary valve replacement in patients with tetralogy of Fallot.

Research at the Proposal Stage

At the proposal stage is a study submitted for approval to the National Pediatric Cardiology Quality Improvement Collaborative examining inter-center variability in hospital length of stay following the Norwood procedure for infants with hypoplastic left heart syndrome. In addition to examining the differences between centers, the research will attempt to determine which center-level factors are associated with different lengths of stay. Funding for this study will be primarily directed towards statistical support, but also may be used for dissemination of data following project completion.

Novel Concepts and Techniques

Investigation into novel techniques has led to extensive discussions between Duke University and Ventripoint (an imaging company, <https://www.ventripoint.com/>), with a recent signed research agreement designating Duke University as the center for validation of this imaging software in single ventricle patients. This imaging technology uses a hardware marker to co-register echo images from multiple echo windows into 3-dimensional coordinates to create ventricular volumes and measure function. Examining the heart in 3-dimensional space from different windows is analogous to the approach used in cardiac MRI, but with the portability, accessibility, and avoidance of sedation that are strengths of echocardiography. The research protocol is under development, with plans to include two prospective arms – one being patients with single ventricles having a routine echocardiogram, and the other being patients with single ventricles having a routine cardiac MRI. If successful, this will open up use of this tool for the clinical assessment of single ventricle patients in all areas – ICU to outpatient.

Lastly, research in the conceptual stage includes the following two projects:

1. Collaboration with Duke Biomedical Engineering to determine ideal aortic arch geometry in single ventricle patients to minimize power loss using real-patient data.
2. Assessing patency of the ductus arteriosus at several short-term time points after delivery prior to initiation of prostaglandin infusion, with the larger goal being to determine safety of longer maternal-infant bonding.



Attachments:

Hill KD et al. A Randomized, Controlled Pharmacokinetic and Pharmacodynamics Trial of Ambrisentan After Fontan Surgery. *Pediatr Crit Care Med* 2020;21:3795-803

Cicioni M et al. Detection of Occult Thrombosis in Individual with Fontan Circulation. Abstract accepted for poster presentation at the American Society of Echocardiography Scientific Sessions 2021