Pediatric Heart Transplant Society

PEDIATRIC HEART TRANSPLANTATION TODAY

PHTS Newsletter

Dr. Juan "Chuck" Alejos, Senior Editor
Dr. Neha Bansal, Junior Editor

February 2025



Dear All,

FEBRUARY IS AMERICAN HEART MONTH!

Wishing you a very happy HEART MONTH! We recognize that Heart disease remains the leading cause of death in the United States. As we pledge to improve the heart health of our kids with a heart transplant, lets also pledge to improve our OWN heart health. Adopting a heart-healthy lifestyle can help you reduce the risk of heart disease and its risk factors. This year, let's take ACTION (no pun intended!) to protect our hearts by getting enough quality sleep, eating better, being active, even if it's a walk in the park with your dogs, once this loooong winter is over! We want to be the best versions of ourselves to be able to be better providers for our tiny little patients who need us for a long time. Let's raise awareness amongst each other and motivate ourselves to take tiny little steps this year. We know small tiny daily habits lead to large results.

Let's get physical ;)

Neha and Chuck



Newsletter Junior Editor
Neha Bansal, MD
Mount Sinai Medical Center



Newsletter Senior Editor
Juan 'Chuck' Alejos, MD
Mattel Children's Hospital

PHTS GROWTH*

12,916 → Patients Enrolled Total
13,311 → Listings/relisting entered
9823 → Transplants entered
420 → Listings for 2024
337 → Transplants for 2024
11 → Listings for 2025
3 → Transplants for 2025

*as of February 1, 2024



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Laura D'Addese, MD
Joe DiMaggio Children's Hospital

The Utility of Early Aspirin Use and the Development of Pediatric Cardiac Allograft Vasculopathy

Despite numerous advancements in all other aspects of pediatric heart transplant (HT) medicine, cardiac allograft vasculopathy (CAV) remains a hurdle to long-term allograft longevity. Immunosuppression medications, de-sensitization therapies, non-invasive monitoring of rejection, and treatment for rejection have all improved. The diagnosis and treatment of CAV, however, has not followed the same trajectory, thus maintaining its position as a leading cause of graft failure and need for retransplantation. Adult studies suggest that early aspirin (ASA) initiation can decrease the risk of CAV. In early 2020, I was a newly minted junior attending reading one of these studies and I wondered if this potential benefit held true in pediatric HT recipients. I submitted a proposal to the PHTS Scientific Committee who thought it was a good question and allowed me and my esteemed co-authors to utilize the PHTS database to try and answer it. The results of that study, "Early aspirin use and the development of cardiac allograft vasculopathy in pediatric heart transplant recipients: A pediatric heart transplant society analysis" and are discussed here, as well as a call for future research.1

Understanding the Challenge: Pathogenesis and Treatment Limitations
The etiology of cardiac allograft vasculopathy is not fully understood. Histologically, it is characterized by progressive, concentric intimal smooth muscle cell proliferation and lipid deposition leading to diffuse luminal stenosis. Risk factors for CAV are well documented and include immunologic and non-immunologic factors that cause endothelial damage and platelet dysregulation, culminating in diastolic dysfunction and graft failure.

The gold standard for diagnosing CAV is coronary angiography. Unlike the focal lesions seen in coronary artery disease, however, the diffuse, concentric nature of CAV makes early detection challenging. While Intravascular ultrasound (IVUS) is more sensitive than angiography at detecting CAV, percutaneous interventions are often not feasible and freedom from graft failure after revascularization is low.2

The Role of Aspirin: Mechanisms and Potential Benefits
Aspirin exerts its effects by irreversibly inhibiting enzyme cyclooxygenase, which is responsible for the production of thromboxane A2, thus reducing platelet aggregation and mitigating the risk of thrombosis. ASA also has anti-inflammatory properties that decrease the production of other inflammatory mediators that contribute to endothelial dysfunction. Adult HTx recipients have more dysregulated platelet aggregation compared to healthy controls, and this dysregulation appears most pronounced in patient with CAV.4 Thus, ASA is an appealing therapeutic target for attenuating CAV. Peled and colleagues demonstrated that early ASA use (defined as ASA initiation within 1-month post-HTx) was independently associated with a reduced risk of CAV and separate studies by Kim et al and Bergmark et al suggested that early ASA use (defined as ≥ 6 months use in the first year) reduced the risk of moderate to severe CAV.4-6

Study Design
This was a 10-year (January 1, 1996 – December 31, 2016) retrospective analysis of the PHTS database. Subjects <17 years of age at the time of primary HTx who survived ≥ 3 years and had at least one annual surveillance cardiac catheterization with coronary angiography and/or IVUS within that period without evidence of CAV were included. Given the known incidence of CAV with time, this age cut-off was chosen to optimize the number of subjects with at least 3 years of follow-up in the database. Patients with a positive crossmatch or undergoing multi-organ or cardiac retransplantation were excluded. Post-HTx surveillance data is submitted to PHTS on an annual basis. Therefore, for the purposes of this study, **"early ASA use"** was defined as ASA initiation within the first 3 years post-HTx and was classified into three categories:

1. **Continuous ASA** present on all annual follow-up forms.
2. **Intermittent ASA** present on at least one annual follow-up form.
3. **No ASA** no documented use during the first 3 years post-transplant.

Key Findings
Of the 9,755 transplants performed during the study period, less than one-third (i.e. 3,011) met the inclusion criteria. ASA use varied from 0% to 100% across centers and 65% of patients received no ASA. The overall incidence of CAV was only 15%, of which two-thirds of patients had only mild (ie ISHLT grade 1) CAV. Contrary to what has been described in adult studies, patients who received continuous ASA had worse freedom from CAV compared to the other groups ($p=0.002$), but with less severe CAV ($p=0.05$). Continuous ASA use was also associated with higher graft loss compared to the other groups ($p<0.001$). There were several differences in baseline characteristics between the continuous ASA continuous ASA and other groups, including older age, higher incidence of myocarditis, lower rate of induction therapy, and higher incidence of rejection. Multiphase parametric hazard modeling did not reveal that ASA use was independently associated with CAV, though it did show that continuous ASA use was independently associated with inferior graft survival compared to the other groups ($p=0.002$). To further adjudicate this finding, we performed propensity score matching after which no significant difference remained between the groups.

Implications, Limitations, and Future Directions
This PHTS study did not demonstrate a protective effect of early ASA use in preventing CAV or graft failure. Disappointing? Sure. Discouraging? Not at all! In fact, the findings in this study could very well hold the key to better delineating the relationship between ASA and CAV in our patients.

First and foremost, the definition of early ASA initiation in this PHTS study differed significantly from that used in the adult literature. This could suggest the presence of beneficial ASA-related effects that are lost if not "activated" at the appropriate time. Second the nature of the PHTS surveillance forms required us to make rather large assumptions about the accuracy of group classifications. For example, patients in the continuous ASA group may have been started on ASA just days before data submission occurred. Conversely, patients may have been on ASA for most of the year, but had it discontinued just prior to data entry into the registry and, therefore, been identified as not receiving ASA. Third, only 15% of participants developed CAV, so the study may have been underpowered to show a protective effect. Nearly two-thirds of the study population never received ASA, which could have further underwhelmed the results.

The wide variability in ASA utilization across PHTS centers was interesting. Given the differences in baseline characteristics, and the fact that continuous ASA remained independently associated with inferior graft survival in multiphase parametric hazard modeling, an underlying selection bias is likely. It is reasonable to imagine that some centers

are fully “proactive” while others are entirely “reactive” in their ASA prescribing practices, leading to higher ASA use in higher risk patients. The small proportion of patients receiving concomitant statins may also have been in this higher risk group, but the potential synergistic effect of combined ASA-statin therapy may have been underrepresented as only 35% of participants were taking statins. Finally, we did not stratify the groups by age, which may have shown a beneficial effect of ASA in older recipients.

Ultimately, this study highlights the need for a standardized approach to patient selection and initiation and maintenance of ASA therapy in pediatric HTx recipients. A prospective, randomized control trial in which ASA is started early (i.e. first 6 months) post HTx is needed to determine its true effect on CAV and graft survival. The PHTS database and network of pediatric HTx centers globally affords the perfect infrastructure for such a venture, and I welcome collaboration from interested centers.

References

1. D’Addese L, Cantor RS, Koehl D, et al. Early aspirin use and the development of cardiac allograft vasculopathy in pediatric heart transplant recipients: A pediatric heart transplant society analysis. J Heart Lung Transplant 2023;42:115-123.
2. Jeewa A, Chin C, Pahl E, et al. Outcomes after percutaneous coronary artery revascularization procedures for cardiac allograft vasculopathy in pediatric heart transplant recipients: a multi-institutional study. J Heart Lung Transplant 2015;34:1163-8. https://doi.org/10.1016/j.healun.2014.11.011
3. de Lorgeril M, Dureau G, Boissonnat P, et al. Increased platelet aggregation after heart transplantation: influence of aspirin. J Heart Lung Transplant 1991;10:600-3.
4. Peled Y, Lavee J, Raichlin E, et al. Early aspirin initiation following heart transplantation is associated with reduced risk of allograft vasculopathy during long-term follow-up. Clin Transplant 2017;31: e13133. https://doi.org/10.1111/ctr.13133.
5. Kim M, Bergmark BA, Zelniker TA, et al. Early aspirin use and the development of cardiac allograft vasculopathy. J Heart Lung Transplant 2017;36:1344-9. https://doi.org/10.1016/j.healun.2017.06.015
6. Bergmark BA, Zelniker TA, Kim M, et al. Early aspirin use, allograft rejection, and cardiac allograft vasculopathy in heart transplantation Clin Transplant 2021;35. https://doi.org/10.1111/ctr.14424



PHTS Live!

March 19, 2025

"Battle of the Protocols"

Matthew Bock MD. - Rady Children's
Madeline Townsend MD - Cleveland Clinic
Laura D'Addese MD - Joe DiMaggio Children's

April 2025 - Date coming soon

"SRTR Survival Calculator"

Speakers announced soon

May 7, 2025

"Health disparities in advanced heart failure therapies"

Khadijah Breathett, MD - Indiana University

June 18, 2025

"Decision making in transplantation: the interplay between science and bias"

Valerie Chepp PhD. - Lerner Research Institute
Cleveland Clinic

Host



Juan Alejos, MD



Manu Varma, D.O.



Lynsey Barkoff, CPNP

PHTS Annual Virtual Leadership Visit



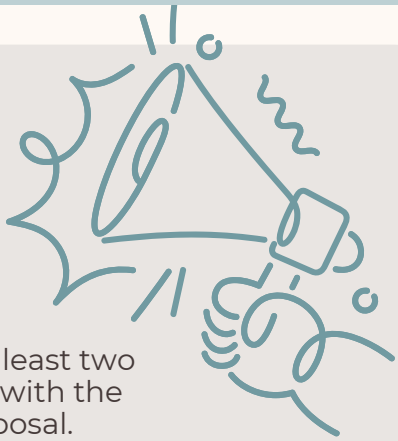
February 27 & February 28, 2025

PHTS Leadership and committee leaders will join to update each other and discuss future projects.

PHTS Proposal Cycles Open

February 1 - 28, 2025

Spring Proposal Cycle **&** **Prospective Proposal Cycle**



If you are considering submitting please contact Claire Covington at least two weeks prior to the proposal deadline so a meeting can be arranged with the Prospective Research Committee to guarantee a successful proposal.

For more information, contact
claire.covington@kirso.net

Enduring Hearts
Healthy Kids ♥ Stronger Hearts ♥ Longer Lives

Member Spotlight



Madeleine Townsend, MD

PHTS Investigator - Enduring Hearts Award Recipient

Donor and Recipient Risk Matching Could Improve Outcomes for All Children Listed for Heart Transplantation



Jennifer Conway, MD

Manuscript accepted for publication in JHLT

Severe Primary Graft Failure: Are there lasting Impacts? Analysis from the PHTS Database



Joseph Atallah, MD

Manuscript accepted for publication in Heart Rhythm

Heart transplantation for pediatric patients with malignant arrhythmias: Indications and Outcomes



Emily Hayes, MD

Manuscript accepted for publication in Pediatric Transplantation

Long-Term Survival in Children Following Heart Transplantation



Shahnawaz Amdani, MD FACC FAAP

Abstract Accepted to American College of Cardiology 2025 Annual Conference

Waitlist and Post-heart Transplant Outcomes for Fontan Patients: An International Multi-center Analysis of Over 1300 Patients



Lydia Wright, MD

Abstract Accepted to ISHLT 2025

DQB1 Donor-Recipient Mismatch and Antibody-Mediated Rejection in Pediatric Heart Transplant Recipients



Waldemar Carlo, MD

Abstract Accepted to ISHLT 2025

Are the Contemporary Outcomes of Older Children with Dilated Cardiomyopathy Supported with Heartmate 3 Equivalent to Those of Heart Transplantation?

PHTS at ISHLT 2025



PHTS Spring Annual Meeting

Sunday, April 27, 2025

Sheraton Boston Hotel

Registration information coming soon

PHTS Mentor and Mentee Lunch

Monday, April 28, 2025

Sheraton Boston Hotel

Registration information coming soon

PHTS and Enduring Hearts Mix and Mingle!

Tuesday, April 29, 2025

Sheraton Boston Hotel

Registration information coming soon



PHTS Booth #229

Make sure to stop by the PHTS Booth at ISHLT!

Sunday, April 27th - Tuesday, April 29th

Job Postings

Faculty position at Norton Children's Hospital/ University of Louisville

Seeking a position for a PEDIATRIC ADVANCED HEART FAILURE AND TRANSPLANT CARDIOLOGIST. Advanced training in pediatric heart failure and transplant required

Contact: Sarah Wilkens at sarah.wilkens@louisville.edu

APP Position at UCSF Benioff Children's Hospital - San Francisco

Join our team at UCSF! Seeking a Pediatric Heart Failure & Transplant APP at UCSF Benioff Children's Hospital San Francisco.

Contact Megan Keating, NP at megan.keating@ucsf.edu with any questions for more information

Pediatric Transplant Cardiologist at Mayo Clinic

The Department of Pediatric & Adolescent Medicine at Mayo Clinic in Rochester, MN, is seeking a Pediatric Transplant Cardiologist to join our practice.

The Pediatric Transplant Cardiologist would join the Division of Pediatric Cardiology within the Department of Pediatric and Adolescent Medicine. The role would primarily be focused on the care of heart failure, mechanical support, and pre- and post-transplant patients. Additional responsibilities include inpatient and outpatient general pediatric cardiology care. The candidate would also have the opportunity to participate in inpatient and outpatient echocardiography depending on experience. The candidate would participate in the general pediatric cardiology hospital service call pool but would only be asked to perform 4-5 weeks per year of general service and call depending on FTE.

Apply here: https://jobs.mayoclinic.org/job/rochester/pediatric-transplant-cardiologist/33647/69801286352

HF/HTx APP position at Primary Children's Hospital (Salt Lake City)

Come join our team! We have two open APP positions for our Heart Failure/Transplant team at Primary Children's Hospital. Having just moved here not too long ago myself, this is a fantastic place to live and work - feel free to reach out if any questions (sharon.chen@hsc.utah.edu)!

Transplant Pharmacist Position

The cardiac, liver, and kidney transplant teams at Primary Children's Hospital in Salt Lake City, Utah are seeking a transplant pharmacist to add to our team of 2 transplant pharmacists and 1 transplant pharmacy technician. This role is 4 ten-hour shifts, no on-call requirement. This pharmacist will be incorporated into the existing monthly rotation, with one pharmacist supporting heart failure and heart transplant, one pharmacist supporting liver and kidney transplant, and one pharmacist supporting outpatient pre- and post-transplant.

Please contact Bridget Bucher (bridget.bucher@imail.org) or Rachel Jackson (rachel.jackson2@imail.org) with questions or to express interest in this position.

Job Postings

OHT/HF position at UCLA Mattel Children's Hospital

UCLA Mattel Children's Hospital Division of Pediatric Cardiology is seeking a Pediatric heart failure and transplantation physician. Applicants should have formal 4th year fellowship training in Pediatric heart failure, cardiomyopathy, transplantation, and mechanical circulatory support and must be board certified/eligible in Pediatric Cardiology. Current trainees are welcome to apply.

Application link: https://recruit.apo.ucla.edu/JPF09362

If you have a job posting that you would like to share with the PHTS Membership, visit the PHTS Basecamp board called Resources for Job Opportunities to add your job posting.