Thoughts from Incoming Fourth Year Fellows

Majid Husain, MD; Ashish Garg, MD; Elizabeth Kalb, MD

As we stand on the threshold of starting our advanced fellowship in pediatric heart failure and transplant, we would like to share our thoughts, motivations, and hopes in pursuing this path. While we come from different institutions and backgrounds, we share a common passion to make a meaningful difference in the lives of pediatric patients battling life-threatening cardiac conditions and to contribute to this field in an impactful way.

In order to do so, we recognize that we must appreciate the rich origin of the field, its inspiring history, current challenges and promising future, the pioneering clinicians of the past and present, along with the courageous patients and their families that have paved the way. On that note, the first successful human heart transplant was performed in 1967 by Dr. Christiaan Barnard in South Africa. However, it was not until the 1980s that pediatric heart transplantation gained traction. Since then, in less than 50 years, the field of pediatric heart failure and heart transplant has advanced significantly, most notably with regards to immunotherapy, rejection surveillance, and mechanical circulatory support. Today, there are almost 500 pediatric heart transplants performed in the United States annually - with 490 pediatric heart transplants in 2021, a 36% increase from just 10 years ago. (1) Along with this increase in volume, there has been an increase in overall survival after transplantation, with patients living longer in the modern era. (2)

Despite the advances in clinical medicine and technology that have led to these improved outcomes in our patient population, we recognize that there is still more work to be done. Specifically, the scarcity of organs continues to be a major problem, the waitlist mortality remains unacceptably high, and the long-time side effects of transplant immunosuppression are a perpetual challenge. Nonetheless, we are optimistic. In the past 3 years of our pediatric cardiology fellowship alone, we have seen incredible progress in the field of xenotransplantation, including transplantation of a genetically modified porcine graft into an adult with nonischemic cardiomyopathy, (3) to provide potential alternatives for selective patients. The expanded use of ABO-incompatible hearts and donation after cardiac death has further increased the donor pool, and optimization of organ transportation perfusion devices (4) continues to reduce the deleterious effects of ischemic time. Furthermore, the field of pediatric mechanical circulatory support has also grown significantly, both in terms of patient volume and innovative strategies to support even the most complex patients. We have also witnessed advances in rejection surveillance, such as the use of donor-derived cell-free DNA technology, (5) that will afford an individualized approach to immunosuppression that may allow for lower but adequate doses of medications and reduce the need for invasive procedures. Collectively, these incremental changes are moving the needle toward improved organ preservation, expanding transplant options, and decreasing waitlist mortality to ensure our patients thrive after heart transplant with minimal complications.

By embarking on this additional fellowship, we seek to acquire knowledge and expertise in providing comprehensive care to our pediatric patients with heart failure. We understand this involves learning the intricacies of disease progression, implementation of effective treatment strategies, and facilitation of timely access to heart transplantation when necessary. In addition to building our foundational knowledge, we aim to conduct research projects aimed at better understanding the patients we treat, the treatments we prescribe, and risks we tolerate. We find inspiration in studies such as the TEAMMATE Trial, the first multicenter randomized clinical trial in pediatric heart transplant aimed at evaluating the safety and efficacy of everolimus and low-dose tacrolimus compared to standard-dose tacrolimus and mycophenolate mofetil. (6) We are looking forward to its clinical findings but also lessons learned in designing and conducting future trials in pediatric heart transplant. We aspire to partake in such projects to develop personalized treatment plans and roadmaps - slowly parting ways from protocolized "one size fits all" strategies. Simultaneously, we will strive to ensure that pediatric patients, regardless of socioeconomic status, have equal access to all available therapies. And, as many more of our transplanted patients are reaching adulthood, we will collaborate with our adult colleagues to ensure that transition programs become standardized and refined.

Thoughts from Incoming Fourth Year Fellows

Majid Husain, MD; Ashish Garg, MD; Elizabeth Kalb, MD

In the immediate future, we also expect to play an active role in improving the short-term and long-term outcomes of our patients with an emphasis on neurodevelopmental measures and quality of life - especially the unique population of Fontan patients and sensitized recipients. We will work on developing guidelines specific to pediatric patients for the management of heart failure and advocating for development of ventricular assist devices made specifically for young children. To aid in this endeavor, we are looking forward to joining PHTS and the ACTION network. In the long-term, we dream that in our careers as transplant clinicians, xenotransplantation or bioengineered hearts becomes routine, where a heart is readily available for whoever needs it and whenever. It may sound far-fetched and something out of a science fiction movie but patients with complex congenital heart disease would no longer have to endure staged palliative surgeries and numerous catheter-based interventions - there would be a personalized heart that could be ordered or taken "off the shelf". We hope waitlist mortality becomes a thing of the past or at least significantly reduced.

Moreover, it's no surprise that the field of pediatric heart failure and transplant thrives on collaboration and the synergy of a multidisciplinary team consisting of pediatric cardiologists, surgeons, advanced practice providers, nurses, transplant coordinators, social workers, pharmacists, psychologists and most importantly the patients we serve and their families. This alliance ensures a holistic and individualized approach that encompasses key aspects of medical, emotional, and psychosocial support for each patient and their families throughout their journey. By capitalizing on this multidisciplinary teamwork, institutional partnerships, precision research, and empathic efforts, we aim to make a lasting impact on the lives of children with heart failure and their families, continually striving for improved outcomes and brighter futures for these young patients.

Lastly, as we begin preparing for the next step in our professional career, we recognize we would not be here without the tremendous guidance from our mentors. Thank you. We are grateful to those who have paved the way for us and feel incredibly humbled to join this field. Additionally, we are excited to become each other's colleagues and look forward to collaborating with each other on future projects.

References:

1. Scientific Registry of Transplant Recipients: OPTN/SRTR 2021 Annual Data Report: Heart. Accessed June 22, 2023. https://srtr.transplant.hrsa.gov/annual_reports/2021/Heart.aspx

2. Rossano JW, Singh TP, Cherikh WS, Chambers DC, Harhay MO, Hayes D Jr, Hsich E, Khush KK, Meiser B, Potena L, Toll AE, Sadavarte A, Zuckermann A, Stehlik J; International Society for Heart and Lung Transplantation. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Twenty-second pediatric heart transplantation report - 2019; Focus theme: Donor and recipient size match. J Heart Lung Transplant. 2019 Oct;38(10):1028-1041. doi: 10.1016/j.healun.2019.08.002. Epub 2019 Aug 10. PMID: 31548029; PMCID: PMC6819143.

3. Griffith BP, Goerlich CE, Singh AK, Rothblatt M, Lau CL, Shah A, Lorber M, Grazioli A, Saharia KK, Hong SN, Joseph SM, Ayares D, Mohiuddin MM. Genetically Modified Porcine-to-Human Cardiac Xenotransplantation. N Engl J Med. 2022 Jul 7;387(1):35-44. doi: 10.1056/NEJMoa2201422. Epub 2022 Jun 22. PMID: 35731912.

4. Naito N, Funamoto M, Pierson RN, D'Alessandro DA. First clinical use of a novel hypothermic storage system for a long-distance donor heart procurement. J Thorac Cardiovasc Surg. 2020 Feb;159(2):e121-e123. doi: 10.1016/j.jtcvs.2019.05.085. Epub 2019 Jul 10. PMID: 31420150.

5. Agbor-Enoh S, Shah P, Tunc I, Hsu S, Russell S, Feller E, Shah K, Rodrigo ME, Najjar SS, Kong H, Pirooznia M, Fideli U, Bikineyeva A, Marishta A, Bhatti K, Yang Y, Mutebi C, Yu K, Kyoo Jang M, Marboe C, Berry GJ, Valantine HA; GRAfT Investigators. Cell-Free DNA to Detect Heart Allograft Acute Rejection. Circulation. 2021 Mar 23;143(12):1184-1197. doi: 10.1161/CIRCULATIONAHA.120.049098. Epub 2021 Jan 13. PMID: 33435695; PMCID: PMC8221834.

6. Almond CS, Sleeper LA, Rossano JW, Bock MJ, Pahl E, Auerbach S, Lal A, Hollander SA, Miyamoto SD, Castleberry C, Lee J, Barkoff LM, Gonzales S, Klein G, Daly KP. The teammate trial: Study design and rationale tacrolimus and everolimus against tacrolimus and MMF in pediatric heart transplantation using the major adverse transplant event (MATE) score. Am Heart J. 2023 Jun;260:100-112. doi: 10.1016/j.ahj.2023.02.002. Epub 2023 Feb 23. PMID: 36828201.