OPTN Kidney & Pancreas Transplantation Committee Continuous Distribution Workgroup
Meeting Summary
February 12, 2021
Conference Call

Silke Niederhaus, MD, Chair
Rachel Forbes, MD, Vice Chair
Vince Casingal, MD, Chair
Martha Pavlakis, MD, Vice Chair

Introduction

The Kidney & Pancreas Transplantation Committee Continuous Distribution Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 2/12/2021 to discuss the following agenda items:

1. Welcome & Review of Project Goals
2. Recap of 1/29 Meeting
3. Overview of human leukocyte antigen (HLA) Matching
4. Discussion: HLA Matching Data Request

The following is a summary of the Committee's discussions.

1. Welcome & Review of Project Goals

The Workgroup reviewed the scope of the Continuous Distribution project, which is to change allocation from a classification-based system to a points-based system. The Workgroup is currently in the second phase of the project where they will be assigning values to the kidney and pancreas attributes and developing a concept paper.

Summary of discussion:

There was no discussion.

2. Recap of 1/29 Meeting

During the Workgroup's last call, the Workgroup completed discussions regarding pediatric prioritizations and developed a data request that included the following:

- Candidate characteristics by age, race/ethnicity, diagnosis, multi-organ transplant, calculated panel reactive antibodies (CPRA), HLA matching
- Waiting list outcomes (waiting time, transplant rate, waitlist mortality)
- Transplant recipient characteristics by age, race/ethnicity, diagnosis, multi-organ transplant, HLA matching, CPRA, HLA mismatch
- Characteristics of donor used in pediatric transplant by age, race/ethnicity, kidney donor profile index (KDPI)
- Deceased and living donor transplant trends in pediatrics and adults

Summary of discussion:

There was no discussion.

3. Overview of HLA Matching

The Workgroup reviewed what is currently in Organ Procurement and Transplantation Network (OPTN) policy, in regards to HLA matching for kidneys and pancreata.

HLA Matching in OPTN Kidney Policy

HLA matching between the donor and candidates is used to give additional priority to candidates on an individual basis. Sensitization, in the form of CPRA, is also used to grant additional priority on a scaled basis. Increased sensitization corresponds to increased priority points within kidney policy. 0-ABDR mismatch and high sensitization are balanced against each other. Lower KDPI kidneys balance 0-ABDR mismatch and highly sensitized against pediatric priority, donor proximity and estimated post-transplant survival (EPTS). Higher KDPI kidneys balance 0-ABDR mismatch and highly sensitized against donor proximity and blood type.

HLA Matching in OPTN Pancreas Policy

The pancreas allocation score is based on candidate registration and proximity; however, HLA matching is incorporated in sorting for each classification. Body mass index (BMI) and age are also included in each allocation classification.

Summary of discussion:

A member mentioned that they have heard discussion that there will be either a reduction or elimination of the consideration for DR matching in kidneys and was hoping some members could address that. A Workgroup Chair mentioned that this Workgroup should be discussing whether we should increase it, decrease it, or keep it the same; however, for pancreas, there's less data to support the value of DR matching so this may be more of a kidney-based decision.

A Workgroup Chair inquired whether the kidney-pancreas (KP) follows the same rule about HLA and priority that the pancreas does. Staff mentioned that the pancreas allocation priority table is in regards to pancreas, KP and islet transplant.

4. Discussion: HLA Matching Data Request

The Workgroup had initial discussions regarding HLA Matching and was reminded that they would need to develop a rating scale to assign points to HLA matches and determine how much weight HLA matching would have within the overall composite allocation score.

The Workgroup was presented with the following questions to consider when making these decisions:

- How much should HLA matching contribute to a candidate's allocation score?
- Which HLA matches should be prioritized?

Summary of discussion:

A member mentioned that, after the kidney allocation score (KAS) was implemented, the percentage of overall transplants for 0-ABDR mismatches fell from 8% to 4%. Staff emphasized that this was correct and that it's not a huge proportion of transplants that are going to 0-ABDR mismatch.

A member inquired about how the 0-ABDR mismatches would be impacted with the upcoming acuity circle allocation. A member mentioned that they don't think the percentage of 0-ABDR mismatches will change. A Workgroup Chair mentioned that, when blood type A and B matching were also given a lot of points about 20 years ago, the 0-ABDR mismatches were about 15% of all transplants so it's been continuously decreasing.

A member stated that the Workgroup would need to know the following before they can make an informed decision about prioritizing and scaling HLA matching:

- Who received the 0-ABDR mismatches kidneys?
    - What age group was the recipient in?
    - What was the recipient's outcomes?
- The racial distribution of recipients who received 0-ABDR mismatched kidneys
- The impact that any HLA matching changes would have on any population

A member inquired if the Workgroup had any data on outcomes of 0-ABDR mismatches in African Americans as opposed to Caucasians either at graft half-life or 5 year survival. Staff mentioned that this data was not available, but is something that could be looked at. Staff questioned what this data would provide. The member stated that it would help the Workgroup understand, if the intent is to allow more African Americans to have 0-ABDR mismatches, to what extent it would reduce graft survival in total number of graft years.

A member mentioned that there's a need for a thorough data review, especially since the latest literature shows that DQ matching may be more important than any other types of matching except for 0-ABDR mismatches. The member suggested, if possible, modeling outcomes/survival by race and the different loci in order to compare the different types of matching. The Workgroup could compare these type of matches to the 0-ABDR mismatches and see if there's any benefit or if it disadvantages any other population.

A Workgroup Chair mentioned that some of their research had looked at transplant outcomes with DQ mismatching, but didn't stratify by race, and found that DQ mismatching was associated with lower graft survival independent of the ABDR matching in both living and deceased donor transplants. The deceased donor transplants lost that effect with longer cold ischemic times. Older data shows that over 50% of transplants had acute rejection in the first year and it was difficult to treat, whereas now it's the class 2 mismatching and the chronic antibody mediated rejection transplant recipients are experiencing.

A member stated that an argument for maximizing HLA matching is that if the recipient's graft life is prolonged, then the recipient doesn't return to the list and compete with all other candidates for a second kidney. This applies more among younger recipients than older recipients. A member emphasized that the characteristics the Workgroup needs to weigh against each other are race, age, and the impact of matching in terms of the benefit and the risk of perpetuating disparities.

A member suggested creating a sliding scale, similar to what's used for CPRA, and use it for age and matching. Then donors and candidates could be matched based on a lower age and a longer chance of survival versus being matched based on an older age and decreased chance of survival.

Staff inquired if, since the Workgroup has already identified pediatrics as being a group they want to prioritize, if they should have considerations for lower EPTS patients for similar reasons. A Workgroup Chair stated that they agree with having similar EPTS considerations and that it would make sense with a sliding scale. A Workgroup Chair mentioned that a lot of pancreas recipients, especially younger pancreas alone recipients, may ultimately develop a need for a kidney transplant. In these cases, priority should be given to HLA matching just to prevent the buildup of antibodies that could prevent a second transplant later. A member stated that, in pancreas data, the acute rejection rates are significantly higher than that of kidney alone. So, when talking about candidates with high immune risk, the Workgroup should consider having the benefit of better HLA matching.

A Workgroup Chair stated that, because of the impact of HLA matching on immediate outcomes in the 1980s and 1990s, a lot of benefits were given to a 0-ABDR mismatch and that created a disproportionate

system. The Workgroup Chair inquired whether members agree that the distribution of races on the wait list should be similar to the distribution of races in the transplant population.

Members agreed that the racial distribution should be similar. A Workgroup Chair emphasized that it's up to the Workgroup to keep remembering this goal while looking at data and proposing solutions.

A member mentioned that this data highlights the need for more outreach to minority populations in order to increase the number of donors, so that everybody would have a better chance of someday being able to obtain a 0-ABDR mismatch donor. A Workgroup Chair argued that, in 2019, 14% of African American donors looks consistent with the total U.S. population; however, the overrepresentation in the dialysis population is always going to be a challenge. A Workgroup Chair agreed that outreach for broader donor candidacy and acceptance is important.

A member stated that the Workgroup could achieve this in a way that is both scientific and cognoscente of racial disparities. A member suggested basing this scale on frequency of antigens in the population and in the donor pool. For example, a patient with a rare haplotype would receive more points than a patient with a common haplotype because such matches occur less frequently.

A member stated there should not be a tradeoff between more 0-ABDR mismatches and balancing racial disparities. The member emphasized that all important aspects should be stated explicitly and, from a mathematical standpoint, that it is possible to design scores to ensure certain levels of equity. A member suggested that the racial makeup of the recipients should be made an explicit goal or metric so the Workgroup can start talking about how to design a system that recognizes that.

A Workgroup Chair mentioned that it would be ideal to have optimal HLA matching without harming equity. A Workgroup Chair suggested calling it an equity score and then using that when weighing HLA matching. The Workgroup Chair emphasized that the Workgroup needs to intentionally pay close attention to equity in allocation.

A member mentioned that they think the Workgroup should remain neutral, meaning the Workgroup should address disparities but shouldn't be advocating for more priority for one group over another. A member clarified by stating that when looking at rare phenotype, the organ should be matched to the candidate that has the rare phenotype and that should be weighed more heavily than other factors. It could be weighed on a scale that's looking at frequencies of HLA antigens in the donor population and in the recipient population. This could be scaled mathematically in a way that might equalize the playing field a bit.

Staff informed the Workgroup this idea could potentially address their access concerns. However, this approach may also have an impact on when continuous distribution could be implemented due to its complexity.

A member inquired if the Workgroup knows what the class 2 HLA matching probabilities look like by population. Another member stated that the Workgroup doesn't have that information, but it could be included in the data request.

A Workgroup Chair emphasized that, to continue these HLA matching discussions, the Workgroup will need assistance from the HLA community and the Histocompatibility Committee.

Next Steps:

The Workgroup will review literature surrounding HLA matching and consider the following questions:

- How should HLA matching be handled in continuous distribution?
    - Is there sufficient evidence demonstrating the benefit of HLA matching?

    - Are we prioritizing the right matches now?
    - Which loci should be prioritized?
    - Are there scenarios where matching matters more than others?
- How should the utility of HLA matching and equitable access to transplant be balanced?

Upcoming Meetings

- February 26, 2021 (Teleconference)

Attendance

- **Committee Members**
  - Silke Niederhaus
  - Martha Pavlakis
  - Rachel Forbes
  - Abigail Martin
  - Arpita Basu
  - Beatrice Concepcion
  - Cathi Murphey
  - Dolamu Olaitan
  - Elliot Grodstein
  - Jeffery Steers
  - John Lunz
  - Krista Lentine
  - Loren Gragert
  - Parul Patel
  - Peter Lalli
  - Peter Stock
  - Pradeep Vaitla
  - Raja Kandaswamy
  - Sommer Gentry
  - Deirdre Sawinski
  - Jodi Smith
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Ajay Israni
  - Bryn Thompson
  - Jonathan Miller
  - Nick Salkowski
- **UNOS Staff**
  - Joann White
  - Lindsay Larkin
  - Rebecca Brookman
  - Kayla Temple
  - Ross Walton
  - Alison Wilhelm
  - Amanda Robinson
  - Ben Wolford
  - Courtney Jett
  - James Alcorn
  - Jen Wainright
  - Joel Newman
  - Kelley Poff
  - Kelsi Lindblad
  - Kerrie Masten
  - Nang Thu Thu Kyaw