OPTN Kidney & Pancreas Transplantation Committees Continuous Distribution Workgroup
Meeting Summary
August 20, 2021
Conference Call

Rachel Forbes, MD, Chair
Oyedolamu Olaitan, MD, Vice Chair
Martha Pavlakis, MD, Chair
Jim Kim, MD, Vice Chair

Introduction

The Kidney & Pancreas Transplantation Committee Continuous Distribution Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 8/20/2021 to discuss the following agenda items:

1. Review of Project Goals & Project Approach
2. Review and Discussion: Impact of Human Leukocyte Antigen (HLA) Matching on Graft Failure in Kidney Transplant Recipients
3. Debrief: 8/11 OPTN Histocompatibility Committee discussion
4. Rating Scale Recommendation
5. Wrap Up & Next Steps

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

1. Review of Project Goals & Project Approach

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 reviewing feedback on their concept paper, which is part of the Summer 2021 public comment cycle.

The following is the chronological process of developing the continuous distribution model for kidney and pancreas:

1. Attribute
    a. Discuss each attribute individually
    b. Ex: calculated panel reactive antibody (cPRA)
2. Rating Scale – where the Workgroup is currently
    a. Determine rating scale for each attribute
    b. Ex: Workgroup decides this should be a steep non-linear scale
3. Weight
    a. Determine weight for each attribute compared to other attributes
    b. Ex: Workgroup decides cPRA should count for 5% of total score
4. Build & Adjust
    a. Use Workgroup's decisions to build draft framework and adjust as needed
    b. Ex: Upon review, Workgroup decides to adjust weight to 10% of total score

A member inquired about a question posed in the concept paper regarding waiting time inversion. Staff explained that that question is posed in order for the Workgroup to receive feedback to take into consideration when they get further into rating scale and weighting discussions.

A Chair stated that the wait time inversion refers to the concept that there are some kidney's that are destined for discard, so the kidneys would actually be offered to candidates with the least time on the list.

2. Review and Discussion: Impact of Human Leukocyte Antigen (HLA) Matching on Graft Failure in Kidney Transplant Recipients

The Workgroup reviewed Scientific Registry of Transplant Recipients (SRTR) models from the data request regarding the impact of Human Leukocyte Antigen (HLA) matching on kidney graft failure.

Data Summary:

The following are the conclusions from the All-Loci Model (mutually adjusted):

- Mismatches at the DR locus are most strongly associated with the hazard of graft failure in this cohort
  - Compared with two DR mismatches, having one DR mismatch was associated with a 10.7% lower hazard of any-cause graft failure
  - Having no DR mismatches was associated with a 15.4% lower hazard of any-cause graft failure

Summary of discussion:

Members expressed their surprise by the lack of effect of DQ loci mismatch on the outcomes. An SRTR representative inquired about the rate of missingness of DQ data and whether it had a higher rate than other antigens. The presenter stated they don't remember the rate of missingness, but they believe the data on this cohort was more complete than previous years.

A member inquired how long the patients in these cohorts were followed for patient and graft loss. The presenter stated that the longest duration of time a patient was followed was six years. The member inquired what the average length of follow up was. An SRTR representative stated that, without a huge variation, it would probably be about three years; however, the presenter didn't remember the exact average of length of follow up.

There was no further discussion.

3. Debrief: 8/11 OPTN Histocompatibility Committee discussion

The Workgroup was provided the following debrief from the OPTN Histocompatibility discussion on HLA matching:

- Focus should be on DR antigen level matching and its equity
  - Avoid disadvantaging any population
  - Nothing to support including A, B, or DQ antigen level matching in continuous distribution prioritization
  - 0-ABDR did not seem to have much of an advantage

Summary of discussion:

An SRTR representative mentioned that the notion of having more variables and antigen levels to match would mean that minorities have a harder time getting transplanted.

A Chair stated that they hadn't seen any data in the SRTR presentation on different populations or races and inquired if that will be something that is modeled once the Workgroup chooses certain points and weights for distribution. An SRTR representative stated that that would be appropriate once the Workgroup starts working on the kidney pancreas simulated allocation model (KPSAM).

A Chair summarized that there's no justification for prioritizing 0-ABDR mismatches in continuous distribution; however, from the presentation, there's justification to prioritize avoiding DR mismatches.

4. **Rating Scale Recommendation**

The Workgroup reviewed the following rating scale recommendations:

- o DR antigen matching should be prioritized
  - ▪ Points would be assigned based on the level of HLA mismatching

Summary of discussion:

A member agreed that the Workgroup can make this recommendation, but suggested that the Workgroup carefully evaluate modeling for any possible ill effects on any other populations. If one recommendation advantages one population group over another, then the member suggested that there could be a counter-balance point added to the priority points to allow the benefit of HLA.

A member noted that they aren't sure whether the allocation system has ever awarded candidate biology points to patients with certain HLA types, like what is done for calculated panel reactive antibodies (cPRA) and other factors that make it harder to get a kidney. So, in regards to the counter-balance points, those patients who are predicted to be unlikely to be advantaged by the DR matching would receive some type of additional priority.

Staff explained that this is something the OPTN Histocompatibility Committee did discuss and does have data on how frequent different alleles appear within the population. The OPTN Histocompatibility Committee had worried that this was out of scope of the project since it would require the creation of another calculator, similar to the cPRA calculator.

An SRTR representative cautioned the Workgroup on the limitations of the study and inquired if other literature regarding DQ antigen outcomes was discussed. Staff explained that other literature was discussed by the OPTN Histocompatibility Committee and their concern was that all current literature is based on epitope matching, which is a level of complexity that isn't available at the time of the match run. The OPTN Histocompatibility Committee wanted to focus on the HLA data that is available at the time of the match run, which is antigen level data. The OPTN Histocompatibility Committee felt that likely, in the future, DQ matching or different levels of matching may be useful, but currently there is no capability to use that for deceased donors.

A member stated that the effect of the recommended rating scale for HLA matching is unknown on minority groups. A Chair agreed and stated that there is no objection to the recommended rating scale at this time, but reviewing further data is important when finalizing this decision.

A Chair stated that it might be shocking for some transplant professionals to move away from zero antigen mismatches since the transplants have such good outcomes. The Chair stated that clinical practice and individual perceptions may be ingrained.

A Chair agreed and explained that those perceptions might date back to when zero mismatches received a lot of priority. The Chair wondered if the perception that zero antigen mismatch are a successful transplant stems from the kidneys being transplanted in patients who haven't been on dialysis as long.

Members agreed that, if the data isn't showing much benefit from zero antigen mismatch, then it's reasonable to proceed with the recommendation.

A member inquired what data the SRTR has on pancreas in regards to impact of HLA matching on pancreas outcomes. An SRTR representative stated that there isn't much data due to there not being a good definition for pancreas graft loss, so the SRTR could only look at patient death.

A member stated that they believe this is one of the attributes for pancreas as well, so the easiest way to handle this for pancreas transplant would be to mirror what kidney does. A member stated that they had thought that, for pancreas, the consensus was that the impact of HLA matching for pancreas pales in comparison to the quality of the donor organ.

Members agreed that due to the lack of outcomes data for pancreas, there might not be enough justification to include it as an attribute for pancreas and this recommendation should only be considered for kidney.

A member inquired if there is a plan to disseminate this data. The member explained that this data contradicts what many members of the Workgroup members perceived, so it would be important to share this with the larger transplant community so they understand where the recommendation is coming from. A member agreed about the importance of disseminating this information and suggested that it should be presented in a more robust manner with more studies.

An SRTR representative stated that there was work done in the past where priority points for A and B antigens were dropped and the simulations showed an improvement in access to transplant for minority patients. The SRTR representative suggested putting this data in context with past work to better help the community understand the recommendation.

To summarize, Workgroup members agreed with the recommendation for kidney with the caveat that there would need to be additional information regarding other populations that may be disadvantaged, but decided to remove HLA matching as an attribute for pancreas. Members also agreed that once that information is received, there could be potential adjustment to the rating scale.

There was no further discussion.

Upcoming Meetings

- September 17, 2021 (Teleconference)

Attendance

- **Workgroup Members**
  - Martha Pavlakis
  - Rachel Forbes
  - Jim Kim
  - Oyedolamu Olaitan
  - Silke Niederhaus
  - Abigail Martin
  - Beatrice Conceptcion
  - Caitlin Shearer
  - David Weimer
  - Parul Patel
  - Pradeep Vaitla
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Ajay Israni
  - Bryn Thompson
  - Jon Miller
  - Nick Salkowski
  - Peter Stock
  - Jodi Smith
  - Raja Kandaswamy
- **UNOS Staff**
  - Joann White
  - Rebecca Brookman
  - Anne McPherson
  - Kayla Temple
  - Ross Walton
  - Amanda Robinson
  - Courtney Jett
  - James Alcorn
  - Janis Rosenberg
  - Kaitlin Swanner
  - Kelsi Lindblad
  - Kerrie Masten
  - Lauren Motley
  - Nicole Benjamin
  - Sarah Booker