

OPTN Pediatric Transplantation Committee

Meeting Summary

January 20, 2021

Conference Call

Evelyn Hsu, MD, Chair

Emily Perito, MD, Vice Chair

Introduction

The OPTN Pediatric Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 1/20/2021 to discuss the following agenda items:

1. Continuous Distribution Update
2. Pediatric Heart: Trends in ABOi Transplantation

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

1. Continuous Distribution Update

The Committee reviewed an update on the progress of the Continuous Distribution project and were prompted to discuss how pediatric candidates should be defined in continuous distribution.

Summary of discussion:

A member inquired about the goal of continuous distribution and whether it is focused on increasing equity, decreasing waitlist mortality, or balancing equity with waitlist mortality. Staff stated that in the National Organ Transplantation Act (NOTA) and the Organ Procurement and Transplantation Network (OPTN) Final Rule, it states that there are multiple goals that need to be achieved by the allocation systems. This insinuates that there isn't necessarily one overarching goal that has to be the primary goal and all others are subservient to it, but in fact there needs to be a balance. Staff mentioned that this balance can be found by using multi-criteria decision making, which has its own established methodologies and a whole field of science related to it.

A member inquired if the continuous distribution model takes geography, distance between donor and recipient, out of the equation. Staff explained that geography will still be in the model. For example, the Lung Transplantation Committee spent a lot of time looking at geography for two different purposes: (1) cold ischemic time and post-transplant outcomes and (2) efficiency of the system. In regards to ischemic time, the Lung Transplantation Committee decided not to include geography because there is so much noise in the system that happens either before transporting the organ or after transporting the organ that they weren't able to make a clear enough correlation between cold ischemic time and geography. In regards to efficiency, the Lung Transplantation Committee created an S-shaped scale that demonstrates that the difference between travelling 10 miles and 20 miles is insignificant, but at some point travel becomes more burdensome – including the risk of potential missed flights, weather delays, and increased cost. And then there's also a certain distance where nobody is going to accept the organs due to infeasibility. Staff explained that the next step, after figuring out how to scale geography so it fits into the continuous distribution model, would be to answer how much geography should matter in comparison to the other goals, such as waitlist urgency or post-transplant survival.

A member expressed concern about a continuous distribution model, while different from one organ to another, not including distance because of the issues with ischemic time. Staff explained that, while geography isn't included because of ischemic time, geography is included in placement efficiency conversations. Staff mentioned that the data doesn't show a strong correlation between distance and post-transplant outcomes although transplant professionals intuitively know that there's a relationship. Staff emphasized that geography matters and will be included in the allocation score, it's just a matter of how the organ-specific committees include it in the score and how much weight they place on it.

Staff asked the pediatric committee if there's a clinical reason why, for specific organs, policy defines pediatric as either age at time of match versus age at time of registration. The Committee Chair mentioned that children listed for liver transplant usually require their liver transplant within a certain period of time or else they will die waiting on the list. The Chair explained that the evidence behind keeping kids at a pediatric status is so that they don't suddenly drop to a lower status, disadvantaging them more, even though they're being cared for by the same team.

A member mentioned that there are centers that have listed liver candidates as they approached 18 years old solely to get this advantage; however, the member didn't understand the implications of this advantage. A member stated that they had done a study a few years ago to see if centers were listing candidates younger than 18 to game the system and didn't see that to be happening.

A member stated that they think of pediatric status in terms of whether a disease occurred during the pediatric age range, even if it's still affecting the candidate once they turn 18. The member emphasized that age 18 is a legal boundary and not really applicable to medical diseases. A member mentioned that it can become difficult for some teenagers who had an unusual disease and couldn't access care appropriately or couldn't get to a transplant center in time. The member suggested that it would be nice to see some consideration for looking at the disease process as opposed to the age of the candidate.

The Committee Chair asked members with lung and kidney expertise if there's a reason that they would prefer candidates to have pediatric priority based on age at time of match versus age at time of registration. A member explained that, for kidney, there is a pediatric priority if the candidate is registered before 18, but there is also match points.

Staff explained that kidney uses both age at time of match and age at time of registration in the allocation system. Lung just uses age at the time of match. Staff also mentioned that some organs currently don't consider pediatrics at all in allocation, so this discussion is also providing advice to those organ-specific committees as they start giving priority to pediatrics.

The Chair stated that the only reason age at time of registration shouldn't be used is to avoid listing pediatric candidates before they need to be listed and then just keeping them listed for a long time. The Chair asked if there could be a phase out, where age at registration is used but then it phases out after the candidate spends some amount of time on the waiting list. The Chair suggested something similar to the 95th percentile amount of waiting list time could be when the phase out starts. Staff mentioned that age is a complicated attribute because there are different laws that need to be considered in terms of age discrimination. Currently, the committees working on continuous distribution are discussing age as a binary choice and have been advised against using a gradation between 0-18 years old; however, staff haven't considered using a gradation of age after 18.

A member noted that a lot of what the Kidney & Pancreas Continuous Distribution Workgroup has been discussing is in regards to attributes that are mostly based on the recipient as opposed to attributes based on the donor. The member explained that some of these donor attributes are addressed indirectly, for instance, centers can put certain size requirements when listing a candidate; however, the age range where the donor attributes become important is in adolescents because the size of those

organs would easily go into someone in their 20s, 30s or 40s. Staff explained that this is an issue across all organs and some organs prioritize pediatric donors so that they are offered to pediatric recipients or vice versa. Staff mention that lung has decided to give a pediatric boost to pediatric candidates for all organs and have also introduced organ sizes and height into the lung continuous distribution model. Staff suggested that, while other organ-specific committees may not adopt the Lung Transplantation Committee's solution, another solution may be to give more points to pediatric donors than adult donors.

A member stated that the word wait list is a misnomer. It applied historically when the wait list was mostly based on time, but, with continuous distribution, essentially every donor has a different "wait list" that pops up based on all of these different attributes. The member also mentioned that there's a misunderstanding both by transplant patients and their families and they think there's a single wait list. A member explained that there's been some discussion regarding this although no decisions have been made regarding a change to the term.

A member mentioned that age 18 is a legal boundary; however, many 18 year olds are more pediatric like than adult like. The member stated that there have also been instances when our society uses 21 as a demarcation and suggested that that may be more appropriate if the Committee needs to consider a hard cut-point to define pediatrics. A member also stated that, in their opinion to justify a pediatric boost, our society believes that there's a lot more life and opportunity ahead of somebody who is 20-22 years old than there is for someone who is 65-70 years old. The Chair mentioned that the post-transplant survival category is, hopefully, where candidates will get recognized for pediatrics in a way that may be more continuous than the current hard boundary.

Members agreed that their ideal definition of pediatric would be the age at the time of disease progression, but, in lieu of that, it would be age at the time of registration instead of age at the time of match.

2. Pediatric Heart: Trends in ABOi Transplantation

The Committee was introduced a new project idea regarding trends in ABO incompatible (ABOi) pediatric heart transplantation.

The concept of ABOi transplantation is that there's natural isohemagglutinins (isoHg), so a patient that is blood type O would eventually have anti-A and anti-B antibodies. At a later age, these antibodies could be prohibitive or could cause injury to a graft that is placed that is of a foreign ABO blood group. However, data shows that these antibodies don't develop uniformly and the earliest age that they've started to develop is 6 months. Since these antibodies develop variably, patients may not naturally make these non-self ABO blood group antibodies until 12 months or 15 months. It's also important to note that if an ABOi organ is transplanted prior to the development of these non-self ABO blood group antibodies, recipients tend not to ever develop them.

Current OPTN ABOi Heart Transplant Allocation Policy:

- Candidates age <1 at time of match run can receive ABOi heart transplant as long as both of the following criteria are met:
 - Listed Status 1A or 1B
 - Reported isoHg titer within prior 30 days
- Candidates older than 1 at time of match but registered before turning 2 can receive ABOi heart transplant as long as one of the following criteria are met:
 - Listed Status 1A or 1B

- Reported isoHg titer of 1:16 or less within prior 30 days and no treatment to lower titer within 30 days of sample collection
- Under age 1, there are no primary or secondary blood group designations for ABOi heart transplant candidates (i.e., blood group of donor is immaterial to organ allocation)
- Age 1-2, ABOi heart transplant is considered a secondary blood group designation (i.e., ABO compatible allocation is favored over ABOi).

Concerns with Current OPTN Policy:

- Current methods to assess titers is relatively insensitive, subjective, and not standardized
- Age at which natural anti A/B/AB production begins is not well defined and varies, including based on blood group
- Fails to account for re-transplant candidates who received ABOi heart transplant and thus able to receive a second ABOi heart transplant
- Successful transplantation across ABO-barrier, even after natural production of isoHgs, including higher than 1:16 titer is reported

Summary of discussion:

Members agreed that this would be a worthwhile project to collaborate on with the Heart Transplantation Committee. Staff mentioned that they would reach out to their colleagues supporting the Heart Transplantation Committee and start facilitating these initial discussions.

Upcoming Meetings

- February 17, 2021 (Teleconference)
- March 17, 2021 (Tentatively In-Person)

Attendance

- **Committee Members**
 - Evelyn Hsu
 - Emily Perito
 - George Mazariegos
 - Abigail Martin
 - Brian Feingold
 - Caitlin Shearer
 - Douglas Mogul
 - Jennifer Lau
 - Johanna Mishra
 - Kara Ventura
 - Sam Endicott
 - Shellie Mason
 - William Dreyer
- **HRSA Representatives**
 - Jim Bowman
 - Marilyn Levi
- **SRTR Staff**
 - Chris Folken
 - Jodi Smith
- **UNOS Staff**
 - Matt Cafarella
 - Rebecca Brookman
 - Betsy Gans
 - Eric Messick
 - James Alcorn
 - Joann White
 - Julia Foutz
 - Kayla Temple
 - Leah Slife
 - Lindsay Larkin
 - Matt Prentice
 - Susan Tlusty
 - Lloyd Board
- **Other Attendees**
 - Elizabeth Spiwak
 - Isa Ashoor
 - Joseph Hillenburg
 - Rachel Engen