

OPTN Pancreas Transplantation Committee Continuous Distribution Workgroup

Meeting Summary

November 20, 2020

Conference Call

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Introduction

The Pancreas Transplantation Committee Continuous Distribution Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 11/20/2020 to discuss the following agenda items:

1. Overview of Project – Review of 11/06 meeting
2. Review and Discussion of Attributes

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

1. Overview of Project – Review of 11/06 meeting

The Workgroup reviewed the scope of the Continuous Distribution project as well as the objectives of the first phase of the project (identifying and categorization of attributes).

Summary of discussion:

During the November 6th meeting, the Workgroup continued their discussions on pancreas-specific attributes and how best to categorize them in the Continuous Distribution model. The Workgroup discussed and included the following attributes to the Continuous Distribution model as follows:

Added to Post-Transplant Outcomes category:

- HLA Matching (0-ABDR)

Added to Candidate Biology category:

- C-peptide (tentative)

Added to Patient Access category:

- Age (pediatric prioritization)

Added to Donor Characteristics category:

- Age (of the donor)
- BMI

There were no comments or questions.

2. Review and Discussion of Attributes

The Workgroup reviewed and discussed proposed attributes and their categorization related to pancreas transplantation for consideration in the Continuous Distribution project.

Summary of discussion:

After an internal review of the attributes proposed by the Workgroup, some clarifying questions were posed to the Workgroup to further specify rationale and categorization of certain attributes. A more simplified version of the category definitions were provided and reviewed by the Workgroup as follows:

- *Medical Urgency:* Amount of risk to a candidate's life or long term health without receiving an organ transplant.
- *Post-Transplant Survival:* A candidate's likelihood of survival for one year after receiving a transplant.
- *Candidate Biology:* Medical characteristics of a candidate can make them harder to match. This can include a candidate's blood type, their body's sensitivity to accepting an organ, or their height.
- *Patient Access:* This addresses transplant access for candidates under the age of 18, as well as *prior living donors*, those who have previously donated an organ or part of an organ.
- *Placement Efficiency:* The amount of resources required to identify a suitable candidate willing to accept the organ and deliver the organ for transplant.

The Workgroup reviewed and provided input on highlighted attributes previously proposed by the Workgroup and their categorization as follows:

Avoiding Organ Wastage

Attribute: Islets

A member stated that islets should be included in the model in order to, at least, let members know that UNOS is involved in islet transplantation. A member explained that the islet field is one way to progress pancreas transplantation and it's important to recognize that one can transplant beta cell function in different ways. A member noted that the majority of pancreas transplants are done for brittle diabetes or in the setting of renal failure. The member emphasized that, from the patient perspective, they would rather undergo an islet transplant at the point when it's equivalent to a pancreas transplant in outcomes.

A member inquired how the Workgroup would translate what's currently in policy into a cliff cut-off in a continuous model.

Another member agreed that the islets should be kept in the pancreas continuous distribution model, since currently there's criteria for when to allocate to islet candidates in policy, and hopefully one day more islet transplants would occur.

United Network for Organ Sharing (UNOS) staff highlighted data that the Workgroup had requested regarding the percentage of islet candidates that are also listed for a pancreas. From 2015-2020, 23.9% (16 out of 67 candidates) of total islet candidates were also listed for a pancreas. A member noted that the current problem is that there is not much funding for islet transplants and there is no reimbursement by insurance. The member explained, however, that funding may occur at any time if companies become interested in researching islet transplantation. The member explained that reimbursement may need to be the first regulation that is changed in order to increase incentive for islet transplants.

A member stated that their vision for islets is that islets will start to be treated as an organ, instead of a drug, and centers can then open islet programs as long as their outcomes are sufficient. Another

member explained that the Workgroup should prepare the pancreas continuous distribution model as if islets are already being treated as organs.

A member inquired if islets fit best under the avoiding organ wastage category. The member explained that post-transplant survival could play into islets and it could also fall under candidate biology. It could fall under candidate biology because patients that have calcified vessels or a frozen abdomen of some sort may be able to receive islet transplants.

Another member inquired whether islets should be considered an attribute or if it should be considered an organ that has its own attributes. The member explained that the way islets come up on the current run is that it goes through all of the pancreas whole graft patients and then it lists patients for islets. Islet patients would be a registered candidate and the Workgroup would have to assign attributes in order to organize and prioritize them. A member stated that the model is not categorizing patients; the model is categorizing donors. A member explained that if there's a pancreas not being used for whole organ transplant, then it's being offered to the islet patients in a sequence that is only based on waiting time at this point, so the question is: How does the Workgroup want the islet patients to rank in order of who it's offered to?

A member mentioned that, historically, some OPOs have listed islet patients as number 1 on the match run ahead of other pancreas whole organ patients only because the pancreas patient's BMI is over 32 and this is how it was designed in policy before. If the BMI is over 32, then the pancreas primary is offered to islets first. However, some OPOs don't do this anymore and are listing islet patients below all pancreas candidates.

A member stated that candidate biology is probably similar among candidates listed for islet transplant and candidates listed for pancreas alone transplant. The member explained that they don't think the islet and pancreas alone candidates are different in any way other than the individual factors that are already being discussed for pancreas alone transplantation by the Workgroup. Some islet recipients will be sicker with age or sicker with autonomic neuropathy or with sensitization. A member noted that all these factors can still be applied to the islet candidate population.

Another member pointed out that the real question is which organs should first go to pancreas whole organ candidates as opposed to islet candidates? A member suggested that, for now, the Workgroup should copy something similar in policy, which is that higher BMI organs should be prioritized to islet candidates and, later on, the Workgroup can negotiate how high that BMI should be.

A member explained that the higher BMI the better it is for islet candidates, as long as the A1c is fine, so there isn't a competition for these pancreas. A member mentioned that sometimes pancreas teams will take pancreas with a higher BMI, extra abdominal, and the pancreas looks normal. A member stated that islets need the fat in the pancreas in order for the digestion and separation to be better. From that standpoint, it makes sense to allocate first to the whole organ recipient, but there may need to be some need for a cut-off.

A member inquired about the amount of time islet programs need to get the pancreas shipped for an islet transplant. A member explained that islet programs need to know ahead of time because they have to schedule the courier, have the OR ready, and only have a 12 hour window to bring the pancreas after cross-clamp and start isolation. Historically, the islet community was fighting to get some organs as primary offer because of the delay, but if the Workgroup can keep the cut-off at a BMI of 32-33 it will help to allocate the organs and it will help islet centers to utilize them by being able to set up logistics from the beginning.

A member mentioned that it sounds like facilitated pancreas allocation is exhausted, then, at that point, islet transplantation should still be considered as an add-on. The member suggested that it may help to notify islet programs at the time facilitated allocation has started to indicate that there may be a pancreas offer and asking how likely it is to get a team together if none of the other whole pancreas centers accept. This would give islet programs more time to prepare and avoiding organ wastage. Members agreed with this idea.

A member inquired whether any members thought that islets should go somewhere other than avoiding organ wastage. A member stated that, based on the last part about facilitated allocation, the Workgroup could potentially put it under placement efficiency.

UNOS staff acknowledged that there is some overlap in the avoiding organ wastage and placement efficiency category definitions and advised that the Workgroup place the attribute in one category that they are able to provide the strongest rationale on.

Workgroup members agreed to leave islets in avoiding organ wastage.

Post-transplant outcomes

Attribute: Facilitated Pancreas

A member stated that they think facilitated pancreas would fit better in just the avoiding organ wastage category. Members agreed that they don't see how it fits in post-transplant outcomes.

Another member suggested renaming the avoiding organ wastage category if the Workgroup is using organs for transplant in that category. Members agreed and stated that the islet is essentially the pancreas and the Workgroup should focus on its life-saving or quality improving characteristics.

Attribute: Distance, Travel

A member stated that if distance and travel were placed under placement efficiency metrics, these attributes would be covered by the Final Rule to use them. While Workgroup members understand and know that these are also surrogates of ischemic time, they are only surrogates. The member continued that the Workgroup knows that distance and travel affects outcomes, but the actual effect on outcomes is mostly dictated by ischemic time. The Workgroup is more covered by the Final Rule, from a legal standpoint, if they move distance and travel into the placement efficiency category.

UNOS staff explained that the Lung Committee also started out with geography in both places: post-transplant outcomes and placement efficiency. The Lung Committee spent a lot of effort trying to see the correlation between distance and travel time, travel time and ischemic time, and ischemic time and post-transplant outcomes. The data wasn't strong enough to predict post-transplant outcomes based upon the distance between a donor hospital and a transplant hospital, so the Lung Committee dropped distance from post-transplant outcomes.

UNOS staff mentioned that with placement efficiency, the Workgroup would need to be clear on what they mean by efficiency of the system – likelihood of acceptance at a certain distance because of ischemic?

A member inquired if any Workgroup members knew of data that supported putting distance under post-transplant outcomes as opposed to placement efficiency or vice versa. A member stated that there are studies that show outcomes were inferior after 16 hours from cold ischemic time (CIT), but travel is a totally different thing. Even when trying to transport a kidney that's a four hour drive, transplant centers will sometimes say they want it to fly and that's 9 hours, which makes distance and travel harder and harder to predict. A member stated that the Workgroup certainly wants the intention to transplant

earlier rather than later for pancreas. A member explained that the pancreas risk index, with cold ischemic time as the strongest correlate, could use distance and travel as surrogate and then that would justify keeping it under post-transplant outcomes.

A member stated that one of the presentations by UNOS mentioned trying to build how they could predict cold ischemia time in their models. A member inquired if there is any way we can do that currently with modeling. UNOS staff said it's something the Workgroup could look into with research and Scientific Registry of Transplant Recipients (SRTR) staff, but mentioned that research or SRTR may not be able to model or predict it. UNOS staff continued by stating that the Workgroup needs a prediction at the moment of deciding how to order the match run, not from the moment of procurement. SRTR explained that this is correct and it's really not distance that explains the cold time, so it's hard to predict.

A member stated that an important point made by UNOS staff was that the Workgroup needs to have this prediction made at the time of allocation. If the Workgroup wants to model something from the time of cross-clamp to when it's going to reach the destination center, then that would be more predictive.

Another member stated that UNOS research had predicted that from the time of allocation (including flights and weather patterns) it would take 7 hours to get it to point A to point B. A member inquired whether there were assumptions made as to what the time of cross-clamp would be. The member continued that if the overall time is broadly divided between allocation and transplantation, then there are two blocks of time: (1) up to the time of cross-clamp and (2) moving forward from cross-clamp. That assumption about time of cross-clamp is where the prediction would be off because it's impossible to predict when teams would be able to go to the OR.

A member mentioned an article discussing import organs with a healthy degree of skepticism based upon ischemia time and remote teams. There was a 2011 AJP paper looking at import vs. local organs based on distance that concluded that it didn't matter whether the organs were imported or not, but the final common pathway was how many hours did it take to transport the organ. A member explained that whatever prolongs cold ischemia time is the final common pathway that affects outcomes.

Another member stated that another paper on islets highlights the differences between local teams versus remote teams procuring organs. The member mentioned that the procurement process was better when a program's own team recovered the organ, even controlling for distance. Another member stated that a program sending their own teams for islet procurement is extremely important, but it was also an effect of the research – the pancreas were treated as a secondary organ. The member emphasized that if procurement is not done properly, then islets won't be available.

A member noted that the Standards committee of the American Society of Transplant Surgeons (ASTS) is working on procurement protocols and putting some guidance for overall organ procurement – order of procurement, time from donation after cardiac death (DCD) to time of clamp to when the liver comes out or when the pancreas comes out. Members agreed that the need for standardization and protocols has never been higher because of transplant programs using remote teams.

A member pointed out that if the organ is going to be utilized, distance and travel are variables that are going to affect ischemia time and become a variable of outcome. However, if distance and travel is going to increase from 16 to 24 hours then it would go into avoiding organ wastage because pancreas programs aren't going to use the pancreas at 24 hours. The member explained that if the organ falls into the utilization threshold then distance and travel are an outcomes issue, but if the organ is sitting on the edge and may drop out of the utilization threshold where it may be wasted then it's an organ wastage issue.

UNOS staff suggested putting travel and distance into both post-transplant outcomes and placement efficiency. UNOS staff mentioned that the Workgroup seems to want to explore modeling the effect of ischemic time on post-transplant outcomes and the Lung Committee has a methodology for how to talk about distance in relation to placement efficiency. Members agreed to keep distance and travel in post-transplant outcomes and adding both attributes to placement efficiency.

Candidate Biology

Attribute: Pancreas after Kidney (PAK)

UNOS staff explained that Kidney's reasoning for putting safety net in patient access was because there is nothing inherent to kidney after liver patients that limits what donors they can accept. The Workgroup has discussed safety net before for PAK patients and categorized it for candidate biology. UNOS staff inquired, based on this information, should PAK stay in candidate biology?

A member stated that the Workgroup put PAK in candidate biology because patients who receive the pancreas after the kidney may need less immunosuppression since they've already been immunosuppressed. Members agreed that moving this to patient access would be more appropriate.

A member stated that, for the future, the Workgroup should consider whether to differentiate PAK patients between pancreas after living donor kidney and pancreas after deceased donor kidney. The member explained that these patients may be very different – one may be preemptively transplanted and contributed a kidney to the kidney list and the other may have been waiting for a long time. Members agreed to make this distinction and put them both in patient access.

Next Steps:

The Workgroup will have a combined meeting with the Kidney Continuous Distribution Workgroup to review proposed pancreas and kidney attributes during the 12/4/2020 meeting.

Upcoming Meetings

- December 4th, 2020 (Teleconference)
- December 18th, 2020 (Teleconference)

Attendance

- **Committee Members**
 - Silke Niederhaus
 - Rachel Forbes
 - Ajay Israni
 - Jeffery Steers
 - Parul Patel
 - Raja Kandaswamy
 - Todd Pesavento
- **HRSA Representatives**
 - Marilyn Levi
- **SRTR Staff**
 - Bryn Thompson
 - Jonathan Miller
- **UNOS Staff**
 - Joann White
 - Amber Wilk
 - Nang Thu Thu Kyaw
 - Rebecca Brookman
 - Ross Walton
 - James Alcorn
 - Kerrie Masten
- **Other Members**
 - Piotr Witkowski