

OPTN Pancreas Transplantation Committee

Meeting Summary

October 9, 2020

Conference Call

Silke Niederhaus, MD, Chair

Rachel Forbes, MD, Vice Chair

Introduction

The Pancreas Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 10/09/2020 to discuss the following agenda items:

1. Islet Wait Time Transfer Request
2. Policy Oversight Committee (POC) Update
3. Research Update: One Year Monitoring of Changes to Kidney-Pancreas Waiting Time Criteria Data Analysis
4. Review and Discussion: Graft Failure Data
5. Project Update and Discussion: Continuous Distribution
6. New Project Ideas

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

1. Islet Wait Time Transfer Request

The Committee reviewed an Islet Wait Time Transfer Request.

- Patient received two failed islet grafts (2016 and 2019)
 - Removed from islet waiting list after second islet transplant
 - Suffers from severe hypoglycemia
- Request: Transfer islet wait time (accumulated waiting time from 10/16/18 listing) to pancreas alone listing

Summary of discussion:

A member wanted to confirm that the patient wanted to accumulate the time from before the second islet. United Network for Organ Sharing (UNOS) staff explained that, from the form, it looked like there was some wait time accumulated from October 16, 2018 that they're requesting to move to the pancreas alone listing.

Members agreed that this request is reasonable – it seems the second islet transplant was a primary non-function and the patient wants to accrue the waiting time from when they were relisted for the islets.

A member noted that when a center is offering islets to a patient it's experimental and transplant surgeons are supposed to do risk indications and explain alternatives to the patient. The member stated that it's important for patients to understand that they're getting a treatment with islets that are not durable and that they're consciously making that decision. This treatment may be best for the patient, but these wait time transfers are disadvantaging another patient who doesn't have that accrued wait time.

A member countered by stating that the Committee doesn't know whether these islet wait time transfers are disadvantaging other patients because the Committee doesn't know the relative waiting time of other patients.

Another member argued that patients that choose islet transplants are also contributing to research and science by getting involved in the trial to advance the field. In this instance, the member stated that the center should put the patient on the pancreas list and proceed with the islet transplant at the same time.

A member inquired how many patients are listed for islet transplant at the moment and how many of those patients are also listed for pancreas. The member suggested that this information would be valuable to the Committee in order to create a guidance document if these wait time transfer requests become more frequent.

All members were in favor of approving this Wait Time Transfer Request.

2. Policy Oversight Committee (POC) Update

The Vice Chair of the Committee presented updates from the POC, including the following:

Strategic Priorities

- Continuous distribution (currently 6 projects)
- Multi-organ allocation (currently 1 project)
- Efficient donor/recipient matching to increase utilization (currently 9 projects)

Pancreas Committee's Involvement in Strategic Policy Priorities

- Continuous distribution – Kidney-Pancreas Committee Continuous Distribution Workgroup is currently working on identifying and categorizing attributes
- Multi-organ allocation – Pancreas representation on Organ Procurement Organization (OPO) Committee's Multi-Organ Workgroup
- Efficient matching – N/A

Summary of discussion:

A member inquired whether the Multi-Organ Workgroup is trying to create a heart-kidney safety net like the safety net for liver or if the workgroup is just focused on the continuous distribution model. A member explained that the workgroup didn't discuss a safety net, but is focused on where to allocate Status 1, 2, and 3 hearts if they also receive a kidney – possibly adjusting the distance to 500 nautical miles (NM) for those patients.

Another member mentioned that when continuous distribution is established there will be discussion about in what order these organs should be distributed.

A member stated that, other than wait time, pancreas doesn't have a validated surrogate marker for who the sickest pancreas or kidney-pancreas (KP) patient is. That will be the biggest challenge to decide whether to approach that at all or stay with wait time in the pancreas continuous distribution model.

Another member mentioned that another challenge would be to ensure pancreas after kidney (PAK) transplants continue to increase as opposed to decrease in the continuous distribution model.

A member suggested that the Committee could use some valuable input or assistance with trying to figure out the factor that contributes to best outcomes after pancreas, SPK or pancreas alone – possibly a score similar to EPTS for kidney that could help quantify post-transplant survival for pancreas patients.

There were no additional questions or comments.

3. Research Update: One Year Monitoring of Changes to Kidney-Pancreas Waiting Time Criteria Data Analysis

The Committee reviewed the following changes made to the Kidney-Pancreas (KP) Waiting Time Criteria:

- BMI and C-peptide thresholds were removed
- A candidate who is registered for a KP and qualifies for kidney waiting time just needs to be on insulin as well to accrue waiting time

Data summary:

- The proportions of Type II diabetic candidates and transplant recipients increases post-implementation
- KP candidate C-peptide and insulin usage stayed roughly the same
- KP candidate BMI increased slightly post-implementation
- KP transplant recipient BMI and C-peptide stayed roughly the same
- The amount of recipients on insulin stayed roughly the same between pre- and post-implementation
- Patient and graft survival decreased as recipient age increased for both pre and post eras

Summary of discussion:

A member mentioned that, when trying to implement this policy, there was concern that there would be gaming or that a significant number of obese Type II diabetic candidates would start to be registered and receive KPs; however, it doesn't seem that this is happening and there has been some increase in access to KP transplants.

Another member noted that there are definitely more KP candidates who have Type II diabetes listed now than there were and there was an increase in BMI. The member stated that the increases in candidate BMI and the number of Type II diabetic candidates isn't excessive and show that surgeons know what they're capable of doing to get reasonable outcomes.

A member pointed out that recipient age is probably the most obvious trait that resulted in differences or better survival for graft and patient survival. The member suggested that this should be something the Committee looks at assigning attributes for pancreas.

A member questioned when the Committee would receive the next monitoring report. UNOS staff stated that it should be after two years.

4. Review and Discussion: Graft Failure Data

The Committee reviewed the 1 Year Post-Policy Monitoring Report for the new pancreas graft failure definition, which went into effect in February 2018.

Data summary:

- Pancreas graft survival is lower in KP recipients post-policy
 - Likely due to changes in definition of graft failure
 - Does not reflect a true decline in pancreas graft survival
- Issues with required data element reported via "status" field and clinical values not reported
- Issues with pancreas graft failure definition threshold
 - 1 or more missing data elements make it unable to calculate
 - Recipient weight no longer on follow up forms

Summary of discussion:

A member inquired what the total number of graft failures were. UNOS staff explained that the number of graft failures is relatively small and that there were a few of these forms that were filtered out because they weren't validated in the system. A member questioned, because these numbers are so small, if it would be worth it to apply for Office of Management and Budget (OMB) approval to add weight back into the follow-up forms and start discussing revisions to the pancreas graft failure definition.

Another member inquired if the "total insulin" question includes basal and short acting insulin combined. UNOS staff explained that it does; however, early on, there were updates to the help documentation to show members what constitutes as insulin and what they should be using for insulin dosage.

A member noted that they thought projects had to go back through OMB approval every three years, so the next approval would be 2021. UNOS staff explained that the project would need to be renewed in 2021 and any requests to make changes would have to go through the Organ Procurement and Transplantation Network (OPTN) data collection process, which would probably put the Committee on a different timeline.

Another member questioned if insulin dose is expressed as an absolute number or if it's expressed as units per kilogram because, even though weight went away, the units per kilogram dosage should take care of the weight equation. UNOS staff explained that they would have to look at the follow-up forms to see what the insulin dose question is asking for.

A member suggested, since there's missing data, setting parameters where the form cannot be completed without filling the insulin dose value in. UNOS staff explained that, while there are potential issues if that field isn't entered, they agreed that they didn't want to create barriers to completing the form and that some data is better than no data.

A member expressed concern that continuing to use insulin and the dosage in the pancreas graft failure definition won't produce long-term reliable data. A member stated that perhaps the Committee created a more complicated definition than they intended. When looking at graft loss, administering 0.5 units/kilogram of insulin per day for 90 days means that the patient has already lost a significant amount of pancreatic tissue and there may be a benefit in having glucagon for some patients. Another member highlighted that the main issue is compliance and accurate data.

A member stated that, while currently units per kilogram of insulin may seem complicated, it was the simpler option when the Committee discussed this in the past.

Another member inquired about what the proportion of people, in terms of failures, were classified by the insulin definition versus (vs.) people that were relisted vs. people that died vs. other. UNOS staff stated that some of that data is in the report, which should be available on the committee SharePoint site.

A member questioned how compliant a center needs to be to maintain the accreditation with the reporting, since the Committee seems to be worried about how challenging collecting the insulin data is. UNOS staff stated this is more of a member quality question, in regards to insulin needs to be reported and what the consequences might be if it's not.

Another member mentioned that they were asked to think about the islet graft failure definition and that the Committee will also need to think about this definition. The member stated that they were

considering using C-peptide in the islet graft failure definition, but it seems more challenging to collect than insulin dosage.

A member noted that, in 2019, A1C and C-peptide fields were added to follow-up forms and that, possibly by next year, the Committee could have enough information on C-peptide to look for correlates in order to determine whether it should be included in the definition. The member emphasized that it will probably be a couple of years before the Committee has the volume of data they need to make analytical decisions.

Another member inquired about the percentage of missing data in this report. UNOS staff explained that it's a relatively large proportion of those that are indicated to be on insulin that are not reporting insulin duration or dosage.

A member suggested the following in order to ensure compliance with filling out the follow-up forms:

- Have the form as totally incomplete and unable to submit unless the center fills out those required fields
- If a center selects "yes" for insulin dose but does not provide value in the next section then the form could default to 0.5 units/kilogram or higher
 - It would count as an adverse outcome for the center
 - This would be a conversation to be had with the IT team

5. Project Update and Discussion: Continuous Distribution

The Committee reviewed the purpose of continuous distribution and the progress that the Pancreas Continuous Distribution Workgroup has made in regards to identifying and categorizing attributes that are specific to pancreas alone.

Summary of discussion:

A member stated that some of these attributes are easier to implement than others. For example, ischemic time is difficult to calculate so the member was not sure how useful that would be in the continuous distribution model. Scientific Registry of Transplant Recipients (SRTR) staff pointed out that they can't model ischemic time and that's something important to keep in mind.

Another member recalled that candidate age had been brought up in previous discussions as a potential attribute for post-transplant survival and stated that it could be an interesting surrogate to use. Members agreed that age should be included under post-transplant survival because there's strong evidence younger recipients are going to get the most benefit, just like for kidney. SRTR staff mentioned that pediatric candidates could be prioritized, but, when it comes to older candidates versus younger candidates, issues related to age discrimination may arise. For example, kidney's EPTS scale used age as a factor among others to calculate post-transplant survival.

A member stated that they supported the idea of prioritizing patients that were prior living donors. A member mentioned that there needs to be a category for recipients of living donor kidney transplants as well.

Another member pointed out that there could be also be a safety net for patients who didn't receive a kidney and have a GFR of 30-40 since they don't qualify for pancreas transplant alone due to risk of kidney failure. This would address one of the biggest dilemmas (marginal kidney function) in solitary pancreas transplantation. A member stated that they weren't sure how the Kidney Committee would think of this, but the Committee could propose this safety net.

A member also stated that diabetic autonomic neuropathy should at least be included in the miscellaneous category, even though it might be hard to quantify.

In regards to placement efficiency, a member mentioned that pancreata are much more likely to be used locally than they are after travelling across the country which causes an increase in discard rates. A member suggested that the Committee could attribute the most points to “local” candidates within continuous and potentially assign a lower weight to this attribute.

Another member then inquired how the Committee would define “local”. A member suggested just basing “local” off of mileage, although mileage alone doesn’t necessarily reflect how far a procurement team travels. Members agreed that, at this time, there isn’t a better way to model distance than mileage.

A member suggested that type of diabetes may play a role of medical urgency. A member stated that post-transplant survival for recipients with Type II diabetes seemed less than for the recipients with Type I diabetes; however, the member concluded that the Committee should get more data surrounding this topic before making their decision.

Another member emphasized that the Committee needs to be careful not to disadvantage patients. If a candidate has diabetes, their access to higher quality, lower KDPI kidneys is limited because having diabetes counts against them in the kidney EPTS score. A member questioned whether this is really fair to sicker patients.

A member noted that hypoglycemic unawareness has come up a lot in the Committee’s discussion surrounding continuous distribution and questioned whether that should be included as a “yes/no” or if the Committee is going to have to come up with a definition for it. A member stated that there are scales and questionnaires that could be used to measure hypoglycemic unawareness; however, there is a potential for gaming the system if centers don’t answer the questionnaires honestly.

Another member suggested that hypoglycemic unawareness could be measured, for those patients on continuous glucose monitors, by the percentage of time the patient is in hypoglycemia during an average day. Members agreed that the details surrounding the use of continuous glucose monitors, especially those that fail or don’t alarm the patient, may be difficult. A member suggested inviting an endocrinologist to join the Pancreas Continuous Distribution Workgroup to help assess these ideas.

A member also suggested using type of diabetes as a surrogate for hypoglycemic unawareness – Type I diabetics are more likely to be at risk of having hypoglycemic unawareness. Members agreed that hypoglycemic unawareness had been in the miscellaneous category due to these complicated problems, but having an expert join the workgroup would be a way to include it in the continuous distribution model.

A member inquired about the importance of the duration of diabetes. A member stated that they weren’t sure where to obtain that information besides the patient’s history. Members agreed that the Committee can circle back to these miscellaneous items (hypoglycemic unawareness, diabetic autonomic neuropathy, type of diabetes, duration of diabetes) and, even if they can’t fit into continuous distribution, potentially fit them into a separate project.

A member inquired about next steps for the continuous distribution project. UNOS staff explained that, once the workgroup has a consensus of the attributes and how they’re appropriately categorized, they will reach out to the Minority Affairs Committee and the Ethics Committee to allow them to provide feedback before the Committee starts developing the continuous distribution concept paper. This concept paper will then be developed and go out for public comment to receive community feedback.

Once the feedback from public comment have been taken into consideration, the Committee will begin developing the prioritization exercise, which is similar to what the Lung Committee was doing during Summer 2020 Public Comment Cycle. This exercise is where the attributes will be prioritized against each other and assigned different weights.

Next Steps:

As the Pancreas Continuous Distribution Workgroup continues to have discussions, the Committee will be updated on the progress of the project and decisions made.

Once the pancreas specific attributes have been finalized, the Pancreas Continuous Distribution Workgroup will reconvene with the Kidney Continuous Distribution Workgroup to discuss continuous distribution as a whole.

6. New Project Ideas

The Committee discussed new potential project ideas, while keeping the POC Strategic Priorities in mind.

Previous Project Ideas

- Rework Graft Failure Definition
- Medical Priority
 - Within the continuous distribution project
 - Being addressed separate from continuous distribution
- Review Islet Wait Time Transfer Request process

Summary of discussion:

A member stated that there's still a lot of interest in pediatric prioritization for pancreas candidates, even potentially before continuous distribution.

Another member proposed a project looking at factors that may influence post-transplant survival after pancreas transplant. The project could analyze the following survival factors:

- Age
- Duration of dialysis for SPK patient
- Creating a score similar to Kidney's EPTS

A member suggested that this could fall under the Medical Priority Workgroup as well and the goal of the workgroup could be efficiency and optimizing placement of organs. Members agreed that currently the Medical Priority Workgroup would be the most feasible project.

Members agreed that it is too early to rework the graft failure definition. A member stated that when the Committee revisits the graft failure definition, they should consider whether they want islet definition to be incorporated into that definition or have a separate definition for islet graft failure.

A member suggested putting in a data request to see how many candidates are listed for islet alone versus islet and pancreas, and using that data to assess whether the Review of Islet Wait Time Transfer Request process would be a viable project.

Next Steps:

- Committee members should send an email showing their interest to join the Medical Priority Workgroup to UNOS support staff

- UNOS staff will gather the requested information regarding Islet Wait Time Transfer Requests and present this during the next Committee call

Upcoming Meetings

- November 18, 2020 (teleconference)

Attendance

- **Committee Members**
 - Silke Niederhaus
 - Ken Bodziak
 - Maria Friday
 - Parul Patel
 - Piotr Wikowski
 - Pradeep Vaitla
 - Raja Kandaswamy
 - Rachel Forbes
 - Shen Luke
 - Todd Pesavento
- **HRSA Representatives**
 - Marilyn Levi
 - Raelene Skerda
- **SRTR Staff**
 - Ajay Israni
 - Bryn Thompson
 - Nick Salkowski
- **UNOS Staff**
 - Brian Plucinski
 - Jen Wainright
 - Joann White
 - Leah Slife
 - Matt Prentice
 - Nang Thu Thu Kyaw
 - Read Urban
 - Rebecca Brookman
 - Ross Walton
 - Nicole Benjamin