OPTN/UNOS Pancreas Transplantation Committee
Meeting Minutes
March 29, 2017
Chicago, IL

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Introduction

The Pancreas Transplantation Committee (hereafter, the Committee) met in Chicago, Illinois on 03/29/2017 to discuss the following agenda items:

1. Broadened ABO Allocation
2. Guidance on Increasing Pancreas after Kidney (PAK) Transplants
3. Maximum Allowable BMI for KP Waiting Time
4. Pancreas Program Functional Inactivity
5. 2 Year Post-Implementation Evaluation of the Pancreas Allocation System (PAS)
6. Pancreas Waiting Time
7. Update on System Optimization Work Group
8. 6 Month Post-Implementation of Facilitated Pancreas Allocation
9. Pancreas Islet Bylaw Requirements

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

1. Broadened ABO Allocation

The Committee reviewed policy language to broaden allocation across identical and compatible ABO blood types in anticipation of sending this proposal to public comment in the fall.

Summary of discussion:

The Committee reviewed the SRTR data analysis that compared different options for prioritizing ABO identical and compatible candidates and reviewed the impact each "run" had on the number of transplants, transplants by blood type, minority and pediatric candidates, and projected years of benefit from transplant.

The results showed that Run 4 had the highest projected median years of benefit from transplant and highest LYFT (life years from transplant) scores. Median years of benefit shows the difference between estimated survival with the transplant versus estimated survival on the waitlist. KP transplants on average have higher LYFT scores than kidney alone transplants, meaning the longevity for the recipient clearly increased. However, the Committee found the presentation of the LYFT scores somewhat confusing in providing aggregate years of benefit for the entire cohort of the waitlist. The Committee asked the SRTR to provide the years of benefit per recipient instead, to make this aspect of the proposal's benefit clearer. The average benefit per transplant would be a little over half a year.

Support for Run 4

In previous discussions, the Committee had agreed that Run 4 was the best option, and members affirmed that decision during the meeting. Run 4 projects a greater increase KP transplants than the projected decrease in kidney alone transplants. Thus, Run 4 indicates the allocation change would provide a net increase in the number of transplants performed, which is Goal 1 of the OPTN. Overall, the new stratification of allocation by blood type brings pancreas

allocation in line with other organs that stratify by blood type. This change promotes a more efficient allocation matching system.

A2 and A2B to B Recipients

One of the changes in Run 4 would allow A2 and A2B blood type donors into type B candidates, since this combination is compatible under the new allocation system. The Committee discussed the compatibility of A2/A2B to B by organ type. For kidney the results are positive. However, the Chair stressed the importance of understanding the outcomes and functionality of grafts for pancreata. There is an abstract indicating similar outcomes for pancreata, but it only reviews the outcomes of four patients. Anecdotal evidence suggests positive outcomes as well, but the Chair indicated that further data analysis may be useful to confirm the likelihood of similar outcomes.

A member noted that a large number of A and AB pancreata go unused, and the opportunity to increase use of these pancreata should be emphasized. One problem for programs is the testing that goes along with the A2/A2B to B compatibility. Another issue is making sure anti-A titers are given to B patients. UNOS doesn't decide what titer protocol should be. A Committee member noted that although there are few A or AB candidates on the waiting list, the allocation change may allow programs to be more aggressive in pursuing transplants.

0-ABDR Mismatch

The Committee discussed whether to remove the 0-ABDR mismatch for type O compatibility. Currently in policy and in programming, O organs go only to O recipients unless the recipient has a zero antigen mismatch. This mismatch requirement would be removed under the policy proposal. The Kidney-Pancreas Simulated Allocation Model (KPSAM) modeling showed that O transplants would be reduced by this change. However, a Committee member noted that the policy change wouldn't loosen the restriction on O donors except within subgrouping of identical and compatible, so only loosening the restriction for people who'd be in the same classification otherwise. Overall, the policy change would increase the number of kidney-pancreas transplants performed, which outnumber the decrease in kidney alone transplants. The KPSAM also showed no negative impact on minority or pediatric populations.

For future review, the Committee may look at 11.4.D in policy to include pancreas in the table allocating blood type for KPs.

Next steps:

The Committee will look at the language again during its upcoming April 10 call to affirm its support for the proposed policy.

2. Guidance on Increasing Pancreas after Kidney (PAK) Transplants

The Committee discussed the current state of pancreas after kidney (PAK) transplants by reviewing data analysis examining PAK outcomes. The data analysis will be formulated as guidance for the pancreas community and will go out for public comment in the fall. The Committee previously discussed this issue at its last in-person meeting in October.

Summary of Discussion

The Committee examined this issue in response to the Venstrom paper, which showed poor outcomes for PAKs but had limitations, including a shorter time frame and a cohort that inappropriately excluded kidney patients with creatinine levels above 2mg/dl. In the years since the Venstrom paper publication the number of PAKs has dropped significantly. The data request and the efforts of the Committee are to examine whether PAKs should be considered more often than they are, to educate the community about the relative risks and when PAKs may be a

good option. The data request extended the time frame to look at 10 year outcomes comparing PAK and Simultaneous Pancreas Kidney transplantation (SPK) with staying on the waitlist. The total cohort included about 30,000 from 1995 to 2010, a greater cohort than was used before. The analysis included inactive patients.

The data showed a pretty similar survival rate for PAK compared to SPK. When looking at hazard ratios, the third panel of PAK showed a hazard increase in the first 90 days, and indicated the procedure wasn't a net benefit overall. The hazard increase in the first 90 days is typical for post-surgical risk after a transplant. The third panel doesn't fully capture the impact of PAKs, however. The panel doesn't show the hazard of having a PAK compared to staying on the waitlist, which markedly changes the outcomes in a positive direction. The 4th panel showed that if the patient got a PAK compared to those waiting for an SPK, a better measure than the 3rd panel of net benefit and long term survival.

The hazard ratio table compared SPK intention to treat (ITT) with PAK intention to treat. However, ITT for SPK differed with ITT for PAK. ITT for PAK included a lot of points of failure - if a candidate got the kidney and failed, or if they died after getting the kidney transplant, or after the pancreas transplant. However there was some discussion in the Committee as to the definition of intention to treat - and the confusion that could come from using it for SPK and PAK when it has different meanings for each. One member said that ITT focused on pre-transplant activity, not on outcomes, since the intention to treat occurs prior to the transplant. Another member countered that ITT should include post-transplant outcomes because they may be indicative of the intention to treat. The research liaison included the fifth panel to adjust for the 4th panel not accounting for patient deaths and pancreas graft failures, but the Committee expressed concern comparing SPK ITT with PAK ITT since SPK ITT doesn't have these failures to compare it to. The research liaison will look at patient survival compared to SPK survival to show a more "apples to apples" comparison.

Another issue discussed with the ITT panels was that the fifth panel (PAK ITT compared to waiting for an SPK) counted certain of the cohort multiple times: someone 90-120 days out from a kidney may be 0-30 days for a pancreas. They'd be classified in the earlier time point, but not counted in the 90-120 day loss. A member noted that patients listed for pancreas transplants have to be healthy enough to be listed, so if the outcome of the kidney transplant was not good, it's unlikely they'd be listed for a pancreas. Another member noted that excluding inactive patients on the pancreas waitlist from the panel's analysis missed a cohort with intention to treat.

The Committee agreed that the ITT comparison with SPK and PAK made the table more confusing to understand. They agreed that the table as previously formulated, showed the relative benefit of having a PAK over a long time period, and the extra column was unnecessary. The Committee also discussed the complexity and difficulty of capturing certain types of patients - for example, it's difficult to capture data on patients who received a kidney and never listed for a pancreas for whatever reason. Only if they relisted would they be captured by the analysis.

The Committee agreed that another important factor was capturing the timing interval between the kidney and pancreas for PAK. Whether the pancreas followed relatively shortly after the kidney, or ten years later, could make a big difference in the patient's post-transplant survival. The research liaison will include this data in the updated analysis.

The Chair noted that in the years after the Venstrom paper was published, centers would sometime get a living donor for a candidate who needed a pancreas and a kidney and purposely not get the pancreas after kidney, for fear of the potentially negative impact. A member suggested the Committee look at the outcomes for live donor kidney recipients who

within a year got a PAK, compared to SPK recipients, living donor kidney recipients with no PAK, and waitlist mortality.

The Committee discussed whether the analysis should look at patient mortality and kidney graft failure, since a concern of the community may be that a PAK may worsen the kidney function or lead to earlier kidney graft failure compared to never getting the pancreas after the kidney. A member suggested not including this in survival analysis but as a separate endpoint to show that kidney graft survival would not be adversely affected by receiving a pancreas after the kidney. The member also suggested showing data on kidney function for PAK versus SPK 1 year or 2 year post kidney. The Vice-Chair agreed, noting that the kidney graft survival definition doesn't include grafts that aren't performing well, so looking at kidney function would show the success of the graft.

Next steps

The research liaison will rework the data analysis to remove the ITT panels and look at patient survival compared to SPK survival to show a more "apples to apples" comparison. The updated analysis will also look at the timing interval between the kidney and pancreas for PAK, patient mortality and kidney graft failure, and kidney function for PAK and SPK recipients.

3. Maximum Allowable BMI for KP Waiting Time

The Committee discussed a project to modify the maximum allowable BMI (body mass index) for KP waiting time. The maximum BMI cannot exceed 30 kg/m2 due to a cap in policy.

Summary of Discussion

The issue under discussion concerns the ability of candidates to be transplanted without KP qualifying criteria. The KP qualifying criteria only allows candidates on insulin with C-peptide less than 2 ng/mL, or candidates on insulin with C-peptide above 2 ng/mL but with a BMI less than or equal to the maximum allowable BMI, to accumulate waiting time. However, 10 candidates listed for a KP but without any waiting time due to a BMI>30 received offers and were transplanted. The Committee reviewed data on the outcomes of these patients.

The liaison discussed how the intent of providing a maximum BMI for the kidney community was to prevent transplanting candidates who are likely to have poor outcomes. When the maximum BMI policy was discussed in public comment, the community did not anticipate that KPs could be transplanted with no wait time. Thus, current policy seeks to prevent a certain action - transplantation of candidates with BMI>30 - and fails; yet that failure does not necessarily lead to the negative outcomes, the fear of which led to the policy in the first place.

So far, there is no mortality in the patients with BMI above the maximum who were transplanted due to the loophole. The data shown to the Committee indicated that waitlist survival for BMI candidates was within 5% regardless of BMI, and the lowest for underweight candidates. The analysis underscores that the overweight patients have similarly positive outcomes compared to other groups.

The Committee discussed whether the KP qualifying criteria should be examined more generally, because it might be arbitrary in the sense that the patients it excludes do not necessarily have worse outcomes. A member suggested looking at the outcomes of patients in the 30-32 BMI group compared to those with BMI 32 and higher. If BMI=30-32 does better than the BMI> 32, that could indicate support for raising the BMI instead of removing the maximum. Several Committee members expressed concern about the Kidney Committee and kidney community's response to removing the BMI maximum entirely. Instead, these members argued for increasing the BMI, to allow for more transplantation of patients while not creating too much consternation in the community.

However, the Chair noted that the language in policy reflects an assumption that more pancreas transplants would be occurring and type-2 diabetics would not be transplanted as they currently are. He recommended removing the restriction on BMI entirely. This would encourage pancreas transplantation and remove a barrier to transplantation that several centers have complained is unnecessary. It would also encourage the transplantation of KPs, who are highest risk of mortality for kidney patients, and include an organ (the pancreas), that often won't be transplanted otherwise. The Chair also noted that no other organ has a similar limitation imposed on it, and it removes discretion from the transplant surgeon arbitrarily. The liaison noted that patients may prove very supportive of a measure removing a barrier to access. UNOS has received feedback from patients confused why 30 is the limit for BMI. A Committee member noted that removing the BMI maximum would remove a burden to review the maximum every 6 months.

The Vice-Chair supported getting data to show whether the removal of the BMI maximum would not lead to indiscriminate use. He indicated it'd be useful to see historical data on KPs with higher BMIs before the current framework was used. This data would illustrate that the number of recipients transplanted with BMIs above 30 is very small, evidence that may reassure the kidney community and other committees. The Committee agreed to look at papers critical of the current policy as part of the process to determine the next steps.

The Committee also discussed whether to modify the requirement to be on insulin in the KP qualifying criteria. The Committee expressed support for modifying this criteria, since members had experienced situations where being on dialysis caused patients to not be on insulin, rendering them incapable of accruing KP waiting time.

The Committee discussed several options for modifying the insulin requirement for KP waiting time:

- requiring insulin dependence OR
- a history of insulin dependence OR
- no insulin dependence at all, but on hypoglycemic agents, which indicate the patient will eventually become insulin dependent

There are issues with modifying the insulin criteria. First, it is unclear what qualifies as insulin "dependence." Similarly, it is unclear what a "history" of insulin dependence might mean: would one shot of insulin qualify? If specified, should the history be for 6 months of insulin use, a year, or longer? Despite these questions, the Committee expressed consensus that a change might be warranted while the Committee is modifying the BMI maximum. The Chair noted that pancreas is one of only two organs that has a waitlist criteria, and the criteria itself may be unnecessary.

In discussion with UNOS staff, the Committee identified a number of criteria that could impact qualifying criteria:

- BMI
- c-peptide
- insulin
- exocrine

The Committee discussed keeping the criteria the same but creating a review group that would evaluate petitions for candidates outside the qualifying criteria and grant exceptions. The liaison noted that this exception process could provide feedback that could lead to a policy change at a future time, but cautioned improving the criteria may be a better option than creating an exception process. UNOS staff advised bringing all the possible solutions to the community to get feedback and determine the best way forward. These possible solutions, to recap, include:

- remove the BMI cap and allow increases
- remove the BMI cap altogether
- modify BMI criteria and other criteria, such as insulin
- remove all criteria
- create an exception review board

The BMI Implementation Subcommittee will continue to discuss these options at its next subcommittee meeting.

4. Pancreas Program Functional Inactivity

The Committee discussed the pancreas program functional inactivity project, which is examining the current and historical impact of low-volume pancreas centers on patient outcomes, as well as the potential impact of closing low-impact pancreas centers on patient access.

Summary of Discussion

The Committee reviewed the history of this project. The MPSC reviews programs that don't transplant a pancreas within a 6 month time period. The MPSC can review programs multiple times. When a program gets flagged, there are a range of options for the MPSC to pursue, ranging from no action to closing the program. The issue of functional inactivity highlights the fact that some programs are performing most of the transplants while some programs perform very few pancreas transplants.

Within the cohort not performing many pancreas transplants, there are geographically isolated centers and those that are close to other pancreas programs. It is the latter the Committee would potentially want to address, since closing down programs in geographically isolated areas may have a negative impact on patient access. For the centers near other pancreas programs, it's unfair for patients to have to wait long at one center and be able to receive a transplant immediately at the other one in the same geographic area. The Chair expressed support for identifying these programs and focusing pressure on them to improve performance of pancreas transplants, possibly by reducing the transplant threshold in the bylaws from a pancreas transplant every 6 months to every 3 months.

Other Committee members expressed concern about closing programs, especially since in other projects (BMI, ABO) the Committee is also focusing on increasing the number of pancreas transplants. It seems antithetical to increase the number of pancreas transplants to close pancreas programs. The Committee discussed a paper showing that the outcomes are similar at low volume programs, but patients wait longer and transplant rates are lower. A member noted that the end result of looking at the data could be a policy change to extend the time period from 6 months to a year, easing the burden on low volume programs.

Next Steps

A subcommittee will meet to discuss a data request to look at potential impact to patient outcomes and patient access.

5. 2 Year Post Implementation Evaluation of the Pancreas Allocation System (PAS)

The Committee has heard an update on the evaluation of the pancreas allocation system (PAS). Part of the implementation plan for that project was six month updates for the first two years, and annually after that. The results presented to the Committee were similar to the data presented to the Committee six months ago in October. The evaluation reviews progress toward five goals the project aimed to achieve:

- increase utilization of pancreas allografts
    - The data showed no statistical difference pre- and post- implementation
- Eliminate disincentives for PAK
    - The data showed no statistical difference pre- and post- implementation
- Standardize the pancreas allocation process to increase access to organs and reduce waiting times for both SPK and pancreas alone (PA) candidates
    - The data showed an increase in donor and transplant volumes
- Develop appropriate qualifying criteria for candidates waiting for SPK transplant
    - Post-implementation registrations went down (2590 to 2510)
- promote appropriate utilization of SPK transplantation after KAS
    - The data showed a similar number of kidney transplants going to SPKs pre- and post- implementation
    - Overall there are more transplants in post implementation era

Next Steps

The Committee decided that since it is pursuing changes to the allocation system, it is no longer necessary to be updated on the PAS evaluation, since that evaluation will be impacted by policy changes going forward.

6. Pancreas Waiting Time

The Committee reviewed a project on waiting time assignments, which can be transferred from other registrations. This waiting time policy was in place pre-KAS, and leads to situations where dialysis time feeds into Kidney, KP, and PA waiting time. The question for the Committee was whether it was fair for KP candidates to have dialysis time go toward their pancreas alone time, when pancreas alone candidates wouldn't have that option. This could lead to situations where a pancreas alone patient registers first but is behind the KP patient because of the KP's dialysis time.

The Committee decided it would be fair, because it allows the KP candidate to get the PAK in the early time frame after getting the kidney. The Committee agreed it would be wouldn't be doing a pancreas alone in a KP, uremic patient. Pancreas alone candidates have a national net to obtain an organ. Because of the availability of import pancreata, pancreas alone candidates have an advantage.

Next Steps

The Committee declined to develop the project further.

7. Update on System Optimizations Work Group

The Committee received an update on the System Optimizations Work Group, which is trying to make organ allocation function more efficiently. The Work Group has discussed creating an additional time limit for final decision for primary and back up centers. The Work Group came up

with donor information to help make a final decision. The presenter noted that for pancreas, final decision is primarily informed by the anatomy and surgical findings.

A Committee member noted that a benefit for improving the allocation process would be to create facilitated placement for other organs (pancreas already has it). This could hasten the time it takes to get the donor into the operating room. The Committee also discussed why the number of organs for final decision would be limited to two: what if another organ offer came in that was better than the other two? In that case, the presenter said, the center could choose the two best organs. The effort of the System Optimizations Work Group seeks to limit the number of organ offers sitting in the ICU, an issue associated with liver allocation. Because of this, the Committee anticipated more feedback from the liver community than the pancreas community, which is less impacted by the proposal.

8. 6 Month Post Implementation Evaluation of Facilitated Pancreas Allocation

In August, the Pancreas Facilitated Allocation proposal was implemented. The research liaison did a pre- and post- 6 month analysis to see its effect. The project was for expedited placement of pancreas allocation, and allowed OPOs the ability to make facilitated offers. In the last six months, 23 OPOs used the facilitated 36 times. A total of 15 pancreata were transplanted, 7 in the post-implementation era. This shows the facilitated process is being utilized, although room for growth exists.

The Committee indicated that future review of this project should also look at the number of donors for the 7 transplants and any more that are performed. The Committee also expressed interest in the overlap between programs participating before the implementation and after. The facilitated programs are reevaluated on an annual basis, so some may carry over and others may not.

Next Steps

The Committee will continue to review facilitated allocation post-implementation in the future, and seek to improve the process further.

9. Pancreas Islet Bylaw requirements

The Committee discussed the pancreas islet program requirements that are currently in the bylaws and whether to change or update these requirements. This discussion stemmed from a memo that the Membership and Professional Standards Committee (MPSC) sent to the Pancreas Committee recommending that the Committee review these personnel requirements.

The Pancreas Committee expressed support for revisiting key islet personnel bylaws and agreed that islet bylaws should require key personnel to have a certain amount of islet-specific experience. In 2013 and 2014, the Pancreas Committee worked on a project to improve bylaw requirements for islet programs and pancreas programs before the project was put on hold. In 2014, the Joint Societies Working Group examined the issue and provided recommendations for changes to pancreas program and islet program personnel requirements. When the Pancreas Committee pursues this project in the future, it will review the work done by the previous Pancreas Committee as well as the recommendations of the Joint Societies Working Group. The project will have to be resubmitted to the POC to become an active project again.

Next Steps

The Committee will revisit the issue on an upcoming call and will keep the MPSC informed of its progress.

Upcoming Meetings

- May 8, 2017 (teleconference)
- June 12, 2017 (teleconference)