

OPTN Kidney Transplantation Committee

Meeting Summary

August 12, 2024

Teleconference

Jim Kim MD, Chair

Arpita Basu, MD, Vice Chair

Introduction

The OPTN Kidney Transplantation Committee (the Committee) met via teleconference on 8/12/2024 to discuss the following agenda items:

1. Looking Ahead
2. Recap: “Hard to Place” Discussions
3. Discussion: Clinical and Cold Ischemic Time Definition of Hard to Place

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

1. Looking Ahead

The Committee received its goal for the day’s meeting is to seek consensus and finalize clinical characteristics of hard-to-place kidneys.

Summary of Presentation:

Committee members were asked to focus on finalizing the proposed clinical characteristics of hard-to-place kidneys. The next steps planned in this effort will then shift the Committee’s focus to apply these clinical characteristics in discussing continuous distribution, addressing both non-use and improving allocation efficiency.

Upcoming meeting dates were shared with the group. Topics to be covered during these meetings include:

- Biopsy Monitoring Reports:
 - 1-Year Review: Established minimum Criteria to Require Biopsy
 - 6-Month Review: Standardize Biopsy Data Collection and Reporting
- Public Comment Proposals:
 - Histocompatibility – Require Reporting of HLA Critical Discrepancies and Crossmatch Events to the OPTN
 - Pancreas- Continuous Distribution Update
- Continuous Distribution: SRTR Modeling Capabilities Update
- Continuous Distribution: Composite Allocation Score Considerations

With a variety of things to be addressed, OPTN Contractor Staff encouraged the group to work efficiently towards its goals as it works to address continuous distribution.

Summary of Discussion:

There was no discussion related to this overview.

2. Recap: “Hard to Place” Discussions

Committee members received a recap of work to date on defining hard-to-place kidneys.

Summary of Presentation:

The original objective of defining hard-to-place kidneys was to develop a preliminary evidence-based definition for kidneys at increased risk of non-use. This definition will be preliminary, such that the committee will be able to modify or tweak this definition as needed after it has been applied for a variety of purposes in this space. The definition will be informed by data and literature.

Through its discussions, a multi-pronged approach has been employed, considering clinical indicators, allocation-based indicators, and cold ischemic time. The Committee has discussed capturing the risk of non-use over time, looking at both clinical and logistical reasons. The Committee’s current public comment update seeks community feedback on anatomical, logistical and allocation characteristics that it seems factor in regarding non-use.

The rationale behind this effort includes:

- Establishing a specific, clear standard for describing which kidneys are “hard to place”
- Identifying which organs are at increased risk of non-use
- Discussing characteristics and potential drivers of non-use that will support the Committee’s development of approaches to improve the likelihood of transplant

It is with this in mind that the committee is asked to focus today’s discussions on finalizing the proposed clinical characteristics of hard-to-place kidneys.

Summary of Discussion:

There was no discussion related to this recap.

3. Discussion: Clinical and Cold Ischemic Time Definition of Hard to Place

Potential applications for the “hard to place” definition were outlined by OPTN Contractor staff as a precursor to the Committee’s discussions.

Summary of Presentation:

A “hard to place” definition may be used in multiple ways, including:

- To modify allocation for kidneys with characteristics associated with non-use
- As a foundation for eligibility criteria for things like expedited placement
- Sharing with the OPTN Expeditious Task Force to help inform their work on addressing non-use

Donor modifiers (e.g. increasing weight on placement efficiency (and reducing distance traveled) for older donors, or those with a longer history of diabetes in order to reduce travel time and associated cold ischemic time) is a good example of this as well as expedited placement (e.g. kidneys in quartile 3 that meet at least two criteria would be eligible for expedited placement). Other project recommendations may also come into play here, such as a request to the Disease Transmission Advisory Committee or the Expeditious Task Force to explore improving the understanding of Hepatitis B and C transmission risk and improving the use of Hepatitis B and C positive kidneys through screening for programs that are willing to use these organs.

The Committee’s literature review was also highlighted alongside review of two OPTN data reports regarding characteristics of non-used kidneys:

- Preliminary data report regarding non-use rates by kidney characteristics

- Adjusted model to understand which characteristics are statistically significant

After review of this second data request, the Committee decided to turn its focus to the highest KDRI quartiles, loosely translating to a KDPI of 50 percent or higher. The fourth quartile of KDPI includes the highest KDPI, 76 to 100 percent. High KDPI was associated with higher non-use rates, particularly when KDPI was 80 percent or greater. For these organs, there was a non-use rate of more than 50 percent. In addition to high KDPI, terminal creatinine, history of hypertension, Hepatitis B or Hepatitis C positive, diabetes of unknown duration or greater than 5 years, donor age, and DCD were also strongly associated with non-use.

OPTN Contractor Staff noted that blood type AB, presence of clinical no or unknown, and history of cigarette use were also found to be statistically significant in association with organ non-use. The Committee discussed these previously, noting that AB blood type was related more to candidate population and relative waiting time more so than donor blood type. The Committee also noted that cigarette use was more relevant to overall donor health and lifestyle, and less directly correlated to impact on graft function. The Committee also noted that it did not feel that the presence of clinical infection was directly clinically relevant to non-use or graft function.

A follow-up analysis was completed to look at the size and frequency of these characteristics in donors with a KDPI of 76-100 percent:

- Terminal creatinine showed a median of 1.20 mg/dl
- 76.11 percent of these donors had a history of hypertension
- Less than 1 percent of the donors were Hepatitis B positive
- 5.95 percent of the donors were Hepatitis C positive
- 5.91 percent of the donors had diabetes for an unknown duration
- 17.89 percent of the donors had diabetes for 5 years or more
- Median donor age of the donors was 61 years
- 46.72 percent of the donors were DCD

In comparison, the following characteristics noted for donors in the third quartile KDRI, with a KDPI of 50-75 percent:

- KDPI 70-79 percent kidneys have a non-use rate of 38.82 percent
- KDPI 60-69 percent kidneys have a non-use rate of 27.53 percent (compared to a 2023 overall non-use rate of 27.18 percent)

It was noted that in this quartile, Hepatitis C positive donors status and diabetes of unknown duration is no longer significant, but kidneys that are biopsied is now included. The Committee had discussed biopsy previously, noting that it was not necessarily the biopsies themselves but rather likely the results appearing on the biopsies.

For this third quartile, the size and frequency of these characteristics in donors with a KDPI 50-75 percent were as follows:

- Terminal creatinine showed a median of 1.04
- 76.64 percent of kidneys were biopsied
- 49.21 percent of donors had history of hypertension
- Less than 1 percent of donors were Hepatitis B positive
- 7.66 percent of donors had diabetes for a duration of 5 years or more
- Median donor age was 51 years
- 46.29 percent of the donors were DCD

The Committee had previously looked at cold ischemic time data as well, noting that risk of non-use is high or highest in the highest KDPI donors regardless of allocation timing. This risk of non-use increases at approximately 5-6 hours post-crossclamp.

To prepare for discussion, several items were flagged as decision points for the Committee's discussion after recognizing that:

- Risk of non-use is highest for the highest KDPI kidneys
- Risk of non-use increases at about 6 hours of cold ischemic time
- Limitations in transportation and logistics can increase risk of non-use
- A greater number of candidate and program declines can indicate increased risk of non-use

Summary of Discussion:

Committee members discussed the value of a definition that captures a large portion of these hard-to-place kidneys in a straightforward manner that is easy to message and understand. Members agreed that it is important to reduce complexity and prioritize practicality, simplicity, and actionability. There was agreement that multiple clinical criteria may make it difficult to get consensus on the definition.

A member questioned some elements of KDPI, noting that biopsy is not part of the KDRI calculation. The Vice Chair noted that KDPI was used for ease of understanding, but the data was based on KDRI quartiles. Committee members suggested that KDPI may not reflect the realities of organ translatability.

One Committee member asked if these elements were all equally weighted, suggesting that a definition might be crafted using 2-3 of the characteristics that have the most influence rather than trying to tie all of them in. The Chair noted that the definition should not rely solely on KDPI, and incorporate additional and specific clinical elements.

A member referenced a paper regarding out of sequence kidney allocation, suggesting that anatomical damage also be included as a characteristic. The member explained that anatomical damage or concerning anatomy can make any organ "hard to place," and in some cases, inappropriate for transplant for most patients. OPTN Contractor staff shared that the current public comment update released by the Kidney Committee does ask a question about anatomy factors with respect to a definition of "hard to place." Feedback has already been received as part of this public comment cycle regarding anatomical damage and surgical damage, and will be reviewed by the Committee at the end of the public comment cycle.

A Committee member remarked on the importance of ensuring the "hard to place" definition is not overly wide, particularly if such a definition is applied to an expedited placement pathway. The member continued that expedited placement should only be used for those organs that may require it in order to ensure use.

The Committee briefly discussed cold time and sequence number without acceptance, and a member proposed that the definition of "hard to place" should incorporate both clinical and logistical characteristics. A member agreed that the definition must be dynamic in order to recognize pre-recovery qualifications versus post-recovery challenges with transparency in the process being a key element. The Vice Chair recommended that the Committee identify 2-3 clinical characteristics for kidneys with KDPI 76-100, as well as anatomy and cold ischemic time factors for lower quartile kidneys. The Vice Chair noted that it will be important to think of this with both expedited placement and continuous distribution in mind.

The Chair suggested that the Committee might agree on the characteristics that were discussed and attempt to define thresholds in an effort to move the discussion forward. Defining the term by KDPI grouping may be too broad. A member stated that if the goal is to define hard-to-place using clinical criteria rather than sequence number or cold ischemic time, then it will be critical to ensure clinical characteristics chosen are data driven to ensure consensus. The member offered that regression analyses could be valuable to determine which factors feature most highly in non-use.

A member asked if the Committee is hoping to define a certain percentage of donor kidneys as “hard to place,” or else capture a certain percentage of the donor population. The member pointed out that in 2023, the overall rate of non-use was 27 percent; if a definition of “hard to place” utilized only KDPI of 50 percent or greater, more than half of the donor population would be considered hard to place, for example. It was noted that the Committee has not discussed a target threshold, but that the Committee would consider and ensure that the definition of “hard to place” referenced an appropriately distributed proportion of the donor population.

In consideration of terminal creatinine, the Committee noted that generally, a normal terminal creatinine is less than about 1.5 or 2 mg/dL. A member offered that creatinine trends may be more informative and useful, as opposed to thresholds. A Committee member noted that there isn’t a focus on terminal creatinine in donor evaluation because acute kidney injury is present as the donor is typically on multiple pressors and inotropes. While nephrologists look for the lowest creatinine, they want to see what the kidney is capable of, and that is usually found earlier in the donor’s hospital course. The member explained that this is also with the assumption that the donor is not on continuous renal replacement therapy, which renders the creatinine value unhelpful in understanding graft function. One member offered that some OPOs will give historical creatinine values to provide additional context. For this reason, terminal creatinine values may not be overly valuable for the hard-to-place definition. Committee members debated whether there was value in keeping terminal creatinine as part of the definition. While statistically significant, its value and the variability in how nephrologists consider it as an element in decision-making varies.

One Committee member recognized that the data reviewed has been from 2023 in terms of predictors of non-use. The member questioned whether there is value in looking at previous years to see if these variables have changed. Another member agreed, noting that the transplant community has become more aggressive over time in the types of organs they are willing to transplant, and better at extending graft life for lower projected longevity organs.

OPTN Contract staff reminded the Committee that this will not necessarily be a final definition, but rather establishing a standard of the community as continuous distribution is being developed. The literature review also looks at non-use trends over time.

Clinical characteristics were noted as perhaps needing additional discussion, as acceptance behavior must also be taken into account.

Discussion next moved to biopsy, recognizing that biopsy criteria are now in place, but some OPOs are still completing biopsies even when not required in an effort to provide additional information that may help place kidneys.

Next Steps:

Additional biopsy data will be shared during the August 26th call that may help the Committee determine whether biopsy should be included in the definition.

Upcoming Meetings

August 26, 2024

September 16, 2024

October 8, 2024 (in person)

Attendance

- **Committee Members**
 - Jim Kim (Chair)
 - Arpita Basu (Vice-Chair)
 - Prince Anand
 - Patrick Gee
 - John Lunz
 - Marc Melcher
 - Jason Rolls
 - Reza Saidi
 - Eloise Salmon
 - Chandrasekar Santhanakrishnan
 - Aparna Sharma
- **HRSA Representatives**
 - James Bowman
 - Marilyn Levi
- **SRTR Staff**
 - Bryn Thompson
 - Jonathan Miller
 - Grace Lyden
 - Peter Stock
 - Jodi Smith
- **UNOS Staff**
 - Kayla Temple
 - Shandie Covington
 - Kaitlin Swanner
 - Sarah Booker
 - Carly Layman
 - Laura Schmitt
 - Ben Wolford
 - James Alcorn
 - Ross Walton
 - Lauren Motley
 - Kimberly Uccellini