OPTN Kidney Transplantation Committee
Meeting Summary
November 15, 2021
Conference Call

Martha Pavlakis, MD, Chair
Jim Kim, MD, Vice Chair

Introduction

The Kidney Transplantation Committee (the Committee) met via teleconference on 11/15/2021 to discuss the following agenda items:

1. Information Technology (IT) Update: UNet℠ Multi-Factor Authentication
2. Establish Minimum Criteria to Require Biopsy Proposal Review and Voting
3. Standardize Pathology Reporting and Data Collection Proposal Review and Voting
4. Predictive Analytics

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

1. IT Update: UNet Multi-Factor Authentication

IT staff presented an update on the Multi-Factor Authentication project, including the roll out plan and preparations UNet users can take.

Data Summary:

Multi-Factor Authentication will be rolled out in 2022. After implementation, utilizing Authy will be required for everyone logging into UNet.

Users can download and setup an Authy account now to ensure there will be no issues after implementation. For questions, visit *https://unos.org/technology/unet/mfa/* or contact the Multi-Factor Authentication support team.

Summary of discussion:

The Committee had no questions or comments.

2. Establish Minimum Donor Criteria Proposal Review and Voting

The Committee reviewed the *Establish Minimum Donor Criteria to Require Kidney Biopsy* proposal recommended by the Biopsy Best Practices Workgroup (the Workgroup).

Data Summary:

The Policy Oversight Committee's (POC) Biopsy Standards Workgroup, established in 2020 to evaluate biopsy practices, identified several key areas of improvement for deceased donor kidney procurement biopsy practices. These key areas resulted in two key Kidney projects: establishing a standard set of donor criteria appropriate for biopsy and developing a standardized pathology report to identify characteristics and data points most useful to inform offer acceptance. The rationale for these projects include the following:

- A standard set of donor criteria for biopsy could reduce unnecessary biopsies, thus increasing offer acceptance efficiency, reduce cold ischemic time, and possibly reduce organ discards
- Standardizing the reporting of characteristics and data points most useful to inform offer acceptance can reduce inconsistencies in analysis and increase allocation efficiency

The Kidney Committee's Biopsy Best Practices developed these projects under the guiding principle that procurement kidney biopsies should be utilized to help determine which patient will receive the most benefit from an organ, and as part of a holistic review of a donor kidney offer.

Currently, biopsy performance rates vary significantly between Organ Procurement Organizations (OPOs), ranging from 28.8 percent to 77.5 percent. The *Establish Minimum Criteria to Require Donor Biopsy* proposal aims to standardize biopsy performance by requirement procurement kidney biopsy for donors who meet a set of proposed criteria, focusing on donor kidneys for which biopsy information could be critical to organ evaluation. This proposal would not limit the OPO to only performing biopsies on donors meeting the proposed criteria.

These criteria were developed utilizing OPTN data, including data on deceased donor kidney biopsies for deceased kidney donors recovered in 2019 by Kidney Donor Profile Index (KDPI), donor age, donor history of diabetes, and Expanded Donor Criteria (ECD). As KDPI and donor age increase, biopsy rates also increase. Similarly, diabetic and ECD donors have higher rates of biopsy. Utilizing this same data, about 28 percent of all deceased kidney donors recovered in 2019 would meet the proposed criteria, 90 percent of which received a kidney biopsy. Of all deceased kidney donors biopsied in 2019, less than half would meet the criteria.

The criteria to require biopsy developed by the Workgroup are:

- Anuria, as indicated by no urine output for at least six consecutive hours
- Renal replacement therapy received during current hospital admission or in the course of donor management
- History of diabetes, or HbA1c of 6.5 or greater during donor evaluation or management
- KDPI greater than 85 percent at time of match run, excluding pediatric donors
- Donor age 60 or older
- Donor age 50-59 and at least two risk factors
    - Hypertension
    - Manner of death: Cerebrovascular Accident (CVA)
    - Terminal creatinine greater than or equal to 1.5

Kidney Disease Improving Global Outcomes (KDIGO) defines the urine output indicator of AKI as "urine volume less than 0.5 ml/kg/h for 6 hours," which could potential be substituted as the definition for the anuria criterion.

<u>Summary of discussion:</u>

The Committee reviewed the Workgroup's proposed policy language. One member pointed out that urine output often varies over time, and is rarely a solid zero across the board, which could eliminate a lot of necessary biopsies. The member continued that the anuria criterion should be more liberal than no urine output for 6 hours, but that the KDIGO urine output threshold is far too liberal. Another member expressed concern about the zero urine output threshold. The Chair agreed, and suggested an output of 100ml in 24 hours, adding that a donor who makes 2ml of urine in 6 hours would still be considered anuric. Another member suggested asking about anuric urine output thresholds in public comment. The Chair agreed.

Staff noted that these criteria represent a minimum of donors that should be biopsied, and that transplant centers may request biopsy for donors outside of this criteria. A member remarked that many OPOs are reluctant to perform biopsies, and could stick very closely to this criteria. The Chair agreed.

The Chair of the Biopsy Best Practices Workgroup shared that the Workgroup struggled with defining anuric urine output thresholds, and that there was concern that too liberal criteria could lead to an increase in unnecessary biopsies. The Chair of the Biopsy Best Practices Workgroup noted that anuria is subjective, and asked the Committee if there was a minimum agreeable threshold. One member remarked that the KDIGO urine output threshold would result in too many biopsies, but that 100ml in 24 hours, while somewhat arbitrary, is a good compromise. The member asked if the Biopsy Best Practices Workgroup discussed any other thresholds. Staff shared that the Biopsy Workgroup felt similarly, and expressed concern about utilizing oliguria, as it could be overly liberal.

A member remarked that the criterion could be "anuria or" a certain number of milliliters per 24 hours, whichever is met first. Another member suggested an average urine output of less than a certain volume for 6 or 24 hours. One member agreed, and asked the Committee what was the least amount of urine in 24 hours that could be defined as acute tubular necrosis (ATN). A member shared that it may be necessary to give a definition of milliliters per kilogram per hour, but that for an adult donor, less than 100ml in 24 hours is reasonable. Several members agreed. The Committee updated the proposed policy language with "anuria, or a urine output of less than 100ml in 24 hours."

Staff responded to a comment regarding high rising creatinine as an indicator of AKI in non-ECD donors, sharing that the Biopsy Best Practices Workgroup discussed creatinine thresholds extensively, and determined that rising creatinine in a donor may not be a sufficient indicator, particularly if there are no other risk factors present.

A member remarked that the anuria criterion should be limited to anuria during donor management as opposed to most recent hospitalization, as this more accurately indicates impacts to kidney function. A donor could have early onset anuria which would not have consequences on kidney function at the time of donor management.

The Chair asked if these criteria could lead to unnecessary biopsies in pediatric donors. One member remarked that anuria could look different in pediatric donors, and suggested including language to exempt pediatric donors for that criterion. The Vice Chair pointed out that pediatric donors generally wouldn't be biopsied, and likely shouldn't be required under a minimum criteria. Another member agreed. The Committee updated the proposed policy language to exclude donors less than 18 years old.

The Committee agreed that this policy proposal would not negatively impact any specific patient populations.

Vote:

The Committee voted unanimously in support of sending the Minimum Donor Criteria to Require Kidney Biopsy proposal to public comment with the finalized proposed policy language below:

2.11.A Required Information for Deceased Kidney Donors

The host OPO must provide *all* the following additional information for all deceased donor kidney offers:

1. Anatomical description, including number of blood vessels, ureters, and approximate length of each

2. Biopsy results, if performed. Biopsy must be performed for kidney donors meeting the criteria below, excluding donors less than 18 years old.
3. Human leukocyte antigen (HLA) information as follows: A, B, Bw4, Bw6, C, DR, DR51, DR52, DR53, DQA1, DQB1, and DPB1 antigens prior to organ offers
4. Injuries to or abnormalities of blood vessels, ureters, or kidney
5. Kidney perfusion information, if performed
6. Kidney laterality

The host OPO must perform a biopsy on deceased donor kidneys from donors that meet *at least one* of the following criteria, excluding donors less than 18 years old.

- Anuria, or a urine output of less than 100ml in 24 hours
- Donor has received hemodialysis or other renal replacement therapy during current hospital admission or in the course of donor management
- History of diabetes, or HbA1C of 6.5 or greater during donor evaluation or management
- KDPI greater than 85% at time of original match run, excluding donors less than 18 years old.
- Donor age 60 years or older
- Donor age 50-59 years, and meets at least *two* of the following criteria:
    - History of hypertension
    - Manner of death: Cerebrovascular Accident (CVA)
    - Terminal serum creatinine greater than or equal to 1.5 mg/dl

3. Standardize Pathology Reporting and Data Collection Proposal Review and Voting

The Committee reviewed the *Standardize Pathology Reporting and Data Collection* proposal recommended by the Biopsy Best Practices Workgroup (the Workgroup).

Data Summary:

The *Standardize Biopsy Reporting and Data Collection* proposal aims to standardize biopsy reporting by establishing a standard set of biopsy parameters and appropriate response to be reported when a procurement kidney biopsy is performed. The proposed parameters are characteristics critical to inform offer acceptance. The response options balance the granularity of information required by evaluating clinicians and the level of details that pathologists of varying levels of expertise can reliably and reproducibly provide. A data collection component is also included, with updates to DonorNet and the Deceased Donor Registration (DDR) form to improve comprehensiveness of and align biopsy data collection.

Pathologist feedback from renal-specific, general, and on-call pathologists included varying recommendations to decrease and increase granularity of responses, removal and inclusion of some parameters, and support for increased clarification.

The Standardized Pathology Report includes the following parameters and response options:

- Biopsy type – wedge or core needle
- Tissue preparation technique – frozen section or formalin-fixed paraffin-embedded (FFPE) section
- Number of glomeruli – open field numerical response
- Number of globally sclerotic glomeruli – open field numerical response

- Percent globally sclerotic glomeruli – open field percentage response
- Nodular mesangial glomerulosclerosis – absent, present, or unknown
- Interstitial Fibrosis and Tubular Atrophy (IFTA) – less than 5 percent, 5-10 percent, 11-25 percent, 26-50 percent, or greater than 50 percent
- Vascular disease (percent luminal narrowing of the most severely involved vessel) – none (less than 10 percent), mild (10-25 percent), moderate (26-50 percent), and severe (greater than 50 percent)
- Cortical necrosis – absent or present with an open field percentage response
- Fibrin thrombi – absent of present with an open field percentage response
- Other comments – open text field

Summary of discussion:

The Chair remarked that the proposed standard pathology report looks reasonable and appropriate.

The Committee determined that this proposal would not have negative impact on any specific patient populations.

Vote:

The Committee voted unanimously in support of sending the Standardize Pathology Reporting proposal to public comment.

4. Predictive Analytics

Staff presented an overview of the DonorNet Predictive Analytics project.

Data Summary:

The DonorNet Predictive Analytics (DPA) Collaboration project has significant potential to improve kidney offer decision-making, which is currently very heterogeneous and arguably one of the most challenging medical decisions.

Suppose a clinician receives a KDPI 75 percent kidney offer for a particular candidate, and a visual is provided with the offer, showing predicted time to next KDPI less than 30 or less than 50 percent offer and the probability of patient death before the next KDPI less than 30 or less than 50 percent offer. This visual would be built via predictive analytics, and can support kidney offer decision making.

The DPA project is the result of a collaboration between Accenture Federal Services and the OPTN. Accenture has engaged with the transplant community, largely focusing on root causes of kidney discards and potential process improvements to the offer acceptance process, including in-depth interviews with patients, transplant surgeons, nephrologists, transplant coordinators and other stakeholders. The OPTN and the United Network for Organ Sharing (UNOS) have been investigating the power of predictive analytics. In 2019, the OPTN System Performance Committee recommended investigating predictive analytics at the time of organ offer, and a UNOS Labs research project has gathered information about current use and perceptions of predictive analytics. This work has resulted in the following salient findings:

- Predictive analytics are desired to support clinical judgement
- The types of analytics of interest broadly are estimated graft function, net benefit, and time to better offer for candidates
- There is a need for transparency regarding the development of these analytics to build trust

The ultimate goal of collaboration is to design predictive analytics that support offer decision-making and can be easily understood by decision-makers, develop these analytic models, build technical

architecture to implement analytics in DonorNet, and deploy them in a pilot study in DonorNet mobile. This approach is multi-disciplinary, utilizing strengths from behavioral science, data science, and tech architecture teams.

Phase I of this project focuses on planning, development, and analysis. Concept testing including resonance testing interviews with six kidney transplant surgeons, one transplant nephrologist, and one transplant center administrator. A behavioral study with 16 simulated offers was also conducted, with participation from 21 kidney transplant surgeons, 4 transplant nephrologists, 25 transplant coordinators or administrators, and 5 others. Phase I showed that displaying predictive analytics impacts offer acceptance decisions, increased consistency in these decisions, and improved confidence levels for decision makers. The study also showed that short times to better offers increased likelihood of refusal, while higher times to better offer increased acceptance.

Phase II focuses on designing, building, and testing. Currently, the predictive analytics visual will display the candidate's time to next offer below 30 and below 50 percent KDPI, probability of death before next offer below 30 and below 50 percent KDPI, and the survival curve for a candidate without transplant. The survival curve and probability of death before next offer are intended to combat optimism bias, in which the transplant team may overestimate the patients' likelihood of surviving on dialysis waiting for a better offer. Initially these will only be displayed for adult kidney candidates.

A collaborative data science team from UNOS and Accenture have produced statistical models to predict time to next offer and waiting list mortality. The preliminary model include factors such as candidate blood type, calculated panel reactive antibody (cPRA), time on dialysis, sequence number on current match run, and other factors for the time to next offer model. The preliminary mortality model includes factors such as candidate age, time on dialysis, body mass index (BMI), diabetes status, diagnosis, and albumin.

The Beta testing for predictive analytics will begin in December at a user level, and will roll out analytics on a small scale to inform the larger pilot roll out in January 2022. The pilot will involve approximately 20 kidney programs, and all DonorNet Mobile users at participating centers will have access to the analytics. The pilot cohort will consider geographic location, urban-surburban-rural divisions, transplant volume, racial diversity of waiting list, DonorNet Mobile usage at the center, and acceptance rates. The pilot and user feedback will inform the development and timeline of a national roll out of analytics. Monitoring will occur over a variety of domains, including participant acceptance and refusal patterns, analytics performance, and user feedback regarding the analytics and performance of the analytic models.

Summary of discussion:

One member expressed support for the predictive analytics tool, and recommended adding higher KDPI options. Staff shared that other feedback has included a third tab for offers of KDPI less than 85 percent.

A member suggested creating a similar version of this tool for patients to see, noting that interpretation still plays a large role, but a similar tool to convince patients to take offers they are called with utilizing data of their likelihood of survival to incoming offers.

One member asked how the KDPI 30 percent and 50 percent were chosen. Staff shared that the original intent was to provide options across the KDPI spectrum, but that became infeasible across the timeframe due to the number of models. The KDPI 30 model includes a sufficiently large sample size and aligns with kidneys prioritized for pediatric patients. The KDPI 50 model was selected as it represents kidneys that were somewhat better than average.

A member asked how sensitive the tool is to transplant center factors, and how the metrics change with allocation changes from circle-based allocation to continuous distribution. Staff remarked that these models are dynamic, especially the time to next offer model. Staff shared that there is a lot of data before the March 2021 removal of DSA policy change, but there is less data available after March 15, 2021, and there is a lot of work being done to build the models and validate them to see how well they validate with and without geography effects in the new era with less data. Staff also noted that the list shown is preliminary and has yet to be finalized, and that the center a candidate is listed at may not have as much effect in the current allocation system. The time to next offer models will need continuous validation and updates as policy changes, while the mortality models are generally more robust and resilient over time to such changes.

Upcoming Meetings

- December 20 – Teleconference
- January 10 – Teleconference

Attendance

- **Committee Members**
  - Martha Pavlakis
  - Jim Kim
  - Amy Evenson
  - Asif Sharfuddin
  - Beatrice Concepcion
  - Caroline Jadlowiec
  - Deirdre Sawinski
  - Elliot Grodstein
  - Erica Simonich
  - Marion Charlton
  - Marilee Clites
  - Peter Lalli
  - Precious McCowan
  - Stephen Almond
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Ajay Israni
  - Bryn Thompson
  - Grace Lyden
  - Jon Miller
- **UNOS Staff**
  - Lindsay Larkin
  - Ross Walton
  - Kayla Temple
  - James Alcorn
  - Jennifer Musick
  - Ben Wolford
  - Chelsea Haynes
  - Darren Stewart
  - Laura Cartwright
  - Lauren Motley
  - Leah Slife
  - Matt Prentice
  - Melissa Lange
  - Mike Ferguson
  - Tina Rhoades
  - Rebecca Marino
- **Additional Attendees**
  - Andy Weiss
  - Dave Weimer
  - Dominick Santoriello