OPTN Lung Transplantation Committee
Meeting Summary
November 17, 2022
Conference Call

Marie Budev, DO, Chair
Matthew Hartwig, MD, Vice Chair

Introduction

The Lung Transplantation Committee (the Committee) met via Citrix GoTo teleconference on 11/17/2022 to discuss the following agenda items:

1. Welcome and agenda
2. Update on feasibility of incorporating registry data into mortality models
3. Lung Composite Allocation Score: Summary Statistics
4. Composite Allocation Score vs. Lung Allocation Score
5. Next Steps and Closing Comments

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

1. Welcome and agenda

The Chair welcomed Committee members and UNOS staff presented an overview of the agenda for the meeting.

Summary of discussion:

There was no further discussion by the Committee.

2. Update on feasibility of incorporating registry data into mortality models

The Committee previously requested that the SRTR evaluate the feasibility of incorporating new variables for cystic fibrosis (CF) and pulmonary hypertension (PH) into the lung mortality models based on registry data.[1] Data for the model would come from the Cystic Fibrosis Foundation Patient Registry and the REVEAL Registry. SRTR staff gave a presentation to the Committee on recent death counts from the OPTN waiting list to check the feasibility.

The cohort was pulled from adult and adolescent (12+ year old) candidates on the OPTN Waiting List from Oct 21, 2019 – Oct 20, 2021. This cohort was selected in order to look at death counts following the introduction of the Trikafta treatment for cystic fibrosis in 2019, since it has reduced the need for lung transplantation in this population. A general rule of thumb is that at least 10 events are needed per variable.

Candidates with cystic fibrosis were pulled from Group C (265 candidates) and had two deaths during the two-year period. After reviewing three potential variables aimed to be added, it was determined that it would take 30 years to reach 30 deaths.

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[1] Summary of October 24, 2022 Lung Transplantation Committee Meeting, OPTN, accessed December 13, 2022, https://optn.transplant.hrsa.gov/media/ecrhgog3/20221024_lung_meeting-summary.pdf.

Candidates with pulmonary hypertension were pulled from Group B (630 candidates) and had 36 deaths during the two-year period. After reviewing five potential variables aimed to be added, it was determined that it would take about three years to reach 50 deaths.

<u>Summary of discussion:</u>

The immediate past Chair said that the introduction of Trikafta would not change the impact of massive hemoptysis frequency of exacerbations on waitlist mortality. SRTR staff stated the variables are real and significant, but the events on the OPTN Waiting List are so rare that it would not be possible to get a good estimate for the waitlist mortality model. The immediate past Chair said the CF registry data has enough events to show the impact even if the OPTN does not have it. SRTR staff said that because the number of mortalities has been so low since the use of Trifakta, there will be low numbers moving forward. Not enough deaths will occur for waitlist mortality to be predicted for 30 years. The Chair asked for the SRTR to consider an expanded cohort with more retrospective information. SRTR staff stated analyzing these variables retrospectively to see if these variables are important enough to add to the mortality models will take six months. They stated the linkage with the CF Foundation is already in process. Linking the REVEAL registry would require additional data use agreement processes.

SRTR staff asked if the OPTN Board of Directors will consider that the mortality rate is not high enough to validate this data collection. The immediate past Chair stated if this can be done retrospectively, she will be in favor of that. She stated she is worried if SRTR does not find a way to incorporate these variables retrospectively, all patients with CF will need an exception request. She hopes to incorporate these variables much sooner than would be possible through prospective data collection.

A member asked how many CF candidates are getting exceptions because this will be a lot of work for a small group of candidates. SRTR staff asked if the number is small enough that an algorithm will be needed for only PH candidates. She noted that the Committee worries that programs are not aware when they will be able to apply for exceptions. The member stated he cannot justify applying point estimates from a different cohort into a new cohort. The new point estimate will be somewhere in the confidence estimates, but it probably will not be the same point estimate pre- and post-Trifakta use. He stated CF patients are much older from a transplant perspective. He asked if it is easier to say that if a patient has massive hemoptysis this will put them in the 90th percentile for waitlist urgency if it is less than 1% of listed candidates. The immediate past Chair agreed and stated the number of CF candidates with exceptions is small, but many candidates have risk events without an exception because programs are not aware that they should be asking for one. Members encouraged education on this topic.

SRTR staff noted the ideal system does not require exceptions because physicians do not always understand the system well enough to file for an exception. The member stated the number of candidates is small enough to just provide this guidance. Members agreed.

<u>Next Steps:</u>

The Committee will see the decision made on the *Update Data Collection for Lung Mortality Models* proposal at the OPTN Board of Directors meeting on December 5, 2022, and then decide how to move forward.

3. Lung Composite Allocation Score (CAS): Summary Statistics

UNOS staff gave an overview of an additional resource of the CAS report and an overview of the national distribution. The report can be found [here.](here)

<u>Summary of discussion:</u>

A member asked about the use of percentage points of 25 points and said it should be based off of the distribution instead of maximum points. UNOS staff responded it is based off percent instead of percentile. The Chair and the immediate past Chair asked whether it is the 90th percentile of waitlist mortality. UNOS staff responded that it is in the clinical guidance for pulmonary hypertension, but in terms of how it is entered in the system, when percentage is entered it will show how many points are requested. The data will be available to request 90th percentile based on the distribution. Members vocalized concern over asking for 90% of the points as opposed to the 90th percentile of the distribution. UNOS staff stated the 90th percentile can be translated from the point value for each specific goal. A member stated it will be helpful to think about percentiles as opposed to absolute score. Members agreed and stated it is easier to understand that people will apply for a percentage of the available points. Justifying the 90th percentile for that subcomponent is harder to understand than a straight percent. The immediate past Chair stated she needs to know how percentiles will affect the other candidates on her list and needs to be able to see this in reference to candidates when requesting a percentile.

The Chair noted the different goals of the score that will be shown are medical urgency, post-transplant outcomes, candidate biology, and patient access to request an exception. She asked if the spread of each goal will be available. UNOS staff explained that distribution will be available.

A member asked if anyone could make any request for an exception. Members stated that people can ask and get guidance from the Committee on how to appropriately submit exceptions. The Chair stated the narrative should support why a patient needs a percentile for an exception but cannot dictate what exception request is made. A member asked if guidance can be given to encourage people to request the 90th percentile for waitlist urgency and post-transplant survival. UNOS staff noted guidance is provided on this already. The Chair stated encouraging others to apply for the 90th percentile will result in additional work. UNOS staff explained that is only the clinical guidance for candidates with pulmonary hypertension, and the Committee can continue to develop guidance for other clinical conditions.

A member asked if there is guidance on how to request an exception for certain conditions. He vocalized concern over equity between centers requesting different exceptions for similar candidates. The members responded that each clinical situation is so different, so it is hard to enforce strict guidance on this. A member stated it may be helpful to see the distribution of candidates' lung allocation score (LAS) now to see if it mirrors the distribution for CAS. The member responded this is significantly different

A member vocalized concern about is the degree to which the distribution of waitlist scores is skewed towards the lower point range. He explained that the exceptions will not be significant because of this. He stated it should not be as shifted as it is towards zero. A member responded that there is a critical lack of knowledge between transplant programs on how and when to ask for exceptions. He stated improved guidance needs to be provided to show the most common exceptions requested to create uniformity in the group, and no allocation system will capture this. The Chair stated it will be helpful to have the immediate past chair of the Committee as the chair of the Lung Review Board and because of this education will be provided.

4. **Composite Allocation Score vs. Lung Allocation Score**

UNOS staff presented on members' concerns that candidates are dropping in rank further than expected in CAS. The objective was to determine correlation between the LAS medical urgency and CAS rank. This was done by examining data from candidates listed as of 11/10/22. UNOS staff ranked candidates' order under LAS and CAS creating scatter plots showing candidates' LAS rank and CAS rank.

Data Summary:

The LAS rank includes candidates ordered by LAS from most medically urgent to least. Rank is assigned by their order, with 1 representing most urgent and highest priority. The CAS rank includes candidates ordered by overall CAS score from highest to lowest. Rank is assigned by their order, with 1 representing highest priority.

The candidate CAS and LAS ranks comparison shows the distribution of the correlation between candidate rate with CAS versus LAS. There is a large spread that shows candidates whose ranks changed significantly. In diagnosis group A, candidates shifted significantly to have higher priority. In diagnosis group B, several candidates who are in the top 25% medical urgency under LAS had their rank change by at least 50 places. In diagnosis group C, there are two candidates with high medical urgency under LAS whose ranks changes by at least 50 places under CAS. One candidate received substantially greater priority. In diagnosis group D, the most medically urgent candidates under LAS experienced a substantial shift downward under CAS. There is still a large cluster of candidates who were prioritized highly under LAS who experienced only a moderate shift under CAS. UNOS staff stated the candidates who have higher post-transplant survival receive higher priority under CAS, even in group D.

Summary of discussion:

The Chair stated under diagnosis group A more patients have a higher priority in CAS and asked for members' thoughts. She stated it is driven by post-transplant survival for chronic obstructive pulmonary disease (COPD) patients. They do not appear as sick on paper as compared to group D even though age is similar. SRTR staff stated they had low priority in LAS and CAS, but it is only less of a low priority. She stated she would only be concerned if they had very high priority under CAS. A member stated that this does not appear to be a one-to-one ratio between waitlist urgency and post-transplant survival, especially in group D. A member responded that is due to confusion over the distribution of candidates rather than the score calculation of candidates.

A member stated age is collinear, for example, group D candidates are generally older and group A candidates are generally younger, so if age is controlled, that would likely explain much of the changing ranks. He explained that all 70+ year old idiopathic pulmonary fibrosis (IPF) candidates who are not likely to live five years have dropped in priority.

A member asked if patients are younger in group D and asked this to be examined. SRTR staff stated the sickest patients are not moving down in priority. Another member argued this is not a one-to-one ratio unless a patient is extremely ill because of the choice of a non-linear curve for the waiting list survival score.

5. **Next Steps and Closing Comments**

The Chair thanked members for joining and stated the Committee will schedule an additional meeting for next week to continue reviewing the CAS analysis.

Summary of discussion:

There was no further discussion by the Committee.

Upcoming Meetings

- November 23, 2022, 12PM EST, teleconference

Attendance

- **Committee Members**
    o Marie Budev
    o Erika Lease
    o Brian Armstrong
    o Cynthia Gries
    o Dennis Lyu
    o Edward Cantu
    o Errol Bush
    o John Reynolds
    o Julia Klesney-Tait
    o Kelly Willenberg
    o Lara Schaheen
    o Matthew Hartwig
    o Nirmal Sharma
    o Pablo Sanchez
    o Soma Jyothula
    o Stephen Huddleston
- **HRSA Representatives**
    o Marilyn Levi
    o Jim Bowman
- **SRTR Staff**
    o David Schladt
    o Katherine Audette
    o Maryam Valapour
    o Nicholas Wood
- **UNOS Staff**
    o Kaitlin Swanner
    o Taylor Livelli
    o Holly Sobczack
    o Krissy Laurie
    o Tatenda Mupfudze
    o Dzhuliyana Handarova
    o Samantha Weiss
    o Sara Rose Wells
    o Susan Tlusty