OPTN Thoracic Organ Transplantation Committee
Continuous Distribution Data Taskforce
Meeting Summary
April 9, 2020
Conference Call

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Introduction

The Thoracic Committee's Continuous Distribution Data Taskforce met via Citrix GoTo teleconference on 04/09/2020 to discuss the following agenda items:

1. Recap
2. Discussion of Attribute Rating Scales

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

1. Recap

UNOS staff presented a recap of the Taskforce's progress to date and summarized the Taskforce's previous decisions:

- Use an integrated analytic approach that aligns pediatric priority I and II with the waitlist urgency measure (WLAUC) and the post-transplant survival measure (PTAUC) and incorporates total ischemia time into the PTAUC model
- Use straight-line distance rather than projected travel distance for rank-ordering lung candidates, with distance serving as a proxy for ischemia time
- Exclude ex vivo lung perfusion (EVLP) transplants when incorporating ischemia time into PTAUC
- Explore larger cohorts for pediatric analyses to increase sample sizes

Summary of discussion:

Taskforce members did not have any questions or comments.

2. Discussion of Attribute Rating Scales

The Taskforce discussed two main topics: the relationship between total ischemia time and one-year recipient survival, and how to predict total ischemia time based on distance for candidates on the match run. The goal of the discussion was to gather more feedback from the Taskforce on these topics to finalize the Continuous Distribution Workgroup data request for SRTR.

UNOS staff described how distance is currently used in the distribution of lungs, and explained that while using distance to estimate ischemia time is not a perfect solution, it is an improvement from the current system that uses hard geographic boundaries to govern allocation.

Summary of discussion:

Relationship Between Ischemia Time and One-Year Survival

SRTR staff presented their analysis on the relationship between ischemia time and one-year survival, which found that ischemia time does not impact outcomes between zero to six hours, but there is a linear increase in risk beyond six hours of ischemia time. SRTR staff asked whether it is appropriate to

incorporate ischemia time into the one-year post-transplant survival model using this analysis, noting that ischemia time is not known at the time that post-transplant survival is estimated for the match run.

Taskforce members expressed concerns that the SRTR analysis does not fully capture the relationship between ischemia time and post-transplant survival. The Vice Chair was not opposed to this approach but noted that the data available through the OPTN is skewed by the decisions made by transplant programs about the organs they are willing to accept. For example, higher ischemia time may not be acceptable to transplant programs in certain circumstances, e.g. with an older donor.

Another member expressed concern about the degree to which predicted outcomes based on imperfect data should influence allocation and preference one patient over another. The member thought that this approach will be difficult to defend unless the data is really reliable. Since there is no difference in outcomes up to six hours of ischemia time, and the difference at eight hours is very small, the member said it would not be appropriate for the OPTN to assign different allocation scores to otherwise equivalent patients based on distance from a hospital. The member acknowledged that the purpose of incorporating ischemia time into the model is to avoid flying organs back and forth, for example, if there are two patients that are equivalent except that one is 10 miles away from the transplant program and one is 300 miles away. The member said that the problem with distinguishing between these two candidates based on distance is that the OPTN does not know that the latter candidate has equal access to organs and the OPTN does not want to prioritize candidates based on how close they live to a hospital. The member opposed placing too much emphasis on predicted outcomes in allocation because the OPTN already holds transplant programs accountable for outcomes, which drives how programs make decisions about organ matches, and transplant programs do this fairly well, since most programs stay in business and have similar outcomes. Given these concerns, the member suggested building these components into the model without giving them much weight so that the model can be strengthened over time as more data is collected.

The Taskforce discussed how this approach differs from the current lung allocation score (LAS) model. A member noted that LAS places more weight on predicted waitlist mortality than predicted outcomes, and clarified that his concern is with the OPTN changing allocation based on predicted survival after transplant, as opposed to the current model in which the transplant programs themselves are empowered to make those decisions by accepting organs that they believe will produce good outcomes. A member responded that the curve depicted by SRTR limits how much ischemia time impacts the allocation sequence until ischemia time is longer than six hours, so this approach probably would not impact candidates within a few hundred miles of each other. The member said that the challenge is accurately predicting ischemia time to ensure that the model produces a fair allocation sequence.

Predicting Total Ischemia Time Based on Distance for Candidates on the Match Run

SRTR staff presented a method for predicting ischemia time based on straight-line distance. SRTR staff explained that since ischemia time is not known at the time of the match run, ischemia time must be estimated based on a variable that is known, like distance. SRTR staff noted that there is a lot of variability in the relationship between ischemia time and distance but there is an upward trend, and the average ischemia time is higher for transplants at 1,000 miles than at 100 miles. The upward trend is mostly linear after 500 miles. SRTR staff asked if the Taskforce is comfortable with this approach, acknowledging that SRTR data does not show much of a relationship between distance and outcomes. SRTR staff said that the challenge is that people believe that ischemia time impacts outcomes, and that longer distance leads to longer ischemia time, which is true on average; but the data varies.

Taskforce members expressed concerns about the high variability in the relationship between ischemia time and distance. Members agreed that at shorter distances, ischemia time differs based on variables

that have nothing to do with distance, like the complexity of the transplant procedure. In these situations, it is the patient's circumstances that dictate the ischemia time and the outcome, not the distance. A member noted that longer ischemia times could impact outcomes in some situations, but this is not reflected in OPTN data because transplant programs do not accept organs when ischemia time is expected to be problematic. The Taskforce discussed possible approaches for incorporating ischemia time in the model that might mitigate these concerns.

Incorporating Ischemia Time at Long Distances

A member said that the Taskforce needs to identify when distance starts impacting outcomes and asked if SRTR evaluated the impact on outcomes at distances over 1,000 miles. SRTR staff explained that they considered a nonlinear relationship between ischemia time, distance, and outcomes to see if it the predictive performance of the post-transplant survival model improved, and the only variable that had an impact was ischemia time. The member concluded that the data shows that ischemia time cannot be predicted by straight-line distance because there are too many other factors that play a role.

HRSA staff pointed out that straight-line distance does predict a minimum ischemia time and the other factors determine the upper bound of the ischemia time. The member responded that the question is whether straight-line distance correlates with the likelihood of the ischemia time being greater than six hours, which is when it impacts outcomes, and the data does not seem to show this correlation.

Another member said that ideally the Taskforce could pick a point where ischemia time is likely to be over six hours – perhaps around 750 miles – though there is still a lot of variability in the data at that distance. The member suggested identifying the distance beyond which transplant programs generally do not accept organs, thereby essentially using likelihood of acceptance to indicate that the ischemia time at that distance is unacceptable. UNOS staff said that other modeling has noted a steep relationship between ischemia time and outcomes starting around five hours, and that one could assume that the vast majority of cases will have over five hours of ischemia time at 1,200 miles. Though the data shows few transplants at that distance, the OPTN match run goes out to 4,000 miles, so this would be one evidence-driven way to ensure that the match run accounts for efficiency and outcomes.

UNOS staff noted that even though there is not a clear inflection point, ischemia time and distance are moving in the same direction in that longer distance leads to longer ischemia time, and increases the likelihood of reaching the six-hour mark. A member noted that higher ischemia time is not always linked to longer distance, explaining that adding a half-hour of travel time is not as bad as adding a half-hour of non-travel time. The patients who were within 200 miles and had higher ischemia times likely had technical problems in the operating room, so the problem is that patients with longer ischemia times and poorer outcomes had other reasons for having poor outcomes besides ischemia time.

A member suggested that SRTR evaluate whether the impact of ischemia time on outcomes goes away at long distances, or evaluate incremental ischemia time for distances beyond 1,000 miles, and if there is no clear impact on outcomes then it is clear that outcomes cannot be predicted accurately by straight-line distance. A member said that while ischemia time is not perfect, distance is a well-known variable, and most people would say there probably should be a difference in allocation score between two otherwise equal candidates if one is 10 miles away and one is 500 or 1,000 miles away. A member said that maybe SRTR can demonstrate that there is a benefit at 250 miles compared to 500 miles, or something along those lines, that would be justifiable based on both practicality and presumed ischemia time. A member responded that the allocation score must be evidence-based and available evidence does not support using straight-line distance to estimate outcomes, though the OPTN has to have something in place to justify not going thousands of miles for a patient with very similar LAS to a closer patient.

The Taskforce ultimately agreed that the Workgroup either needs to have a way to incorporate ischemia time that makes sense, or the Workgroup needs to exclude ischemia time and explain why, particularly since ischemia time can be a surrogate for indicating damage to a donor organ.

Justification for Excluding Ischemia Time

The Taskforce discussed approaches for demonstrating to the community why ischemia time should not be incorporated into the model. A member suggested that SRTR model what the data shows, which is that ischemia time begins to have an impact on outcomes after six hours. The member suggested either doing more modeling to try and find something more predictive than distance, or add something conservative to the model that can be re-evaluated with more data. The member also said that once continuous distribution is implemented, the OPTN will have to assess whether there is a sudden change in outcomes because of the impact of ischemia time as organs travel farther.

Next steps:

SRTR will distribute additional information from their analysis of ischemia time, distance, and post-transplant survival. The Taskforce will continue their discussion of attribute rating scales and will consider how distance should be incorporated into the continuous distribution model without using ischemia time. The Workgroup will receive an update on the Taskforce's discussions to date.

Upcoming Meetings

- April 16, 2020 (Workgroup)
- May 14, 2020 (Data Taskforce)