OPTN Thoracic Organ Transplantation Committee
Continuous Distribution Data Taskforce
Meeting Summary
March 12, 2020
Conference Call

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Introduction

The Thoracic Committee's Continuous Distribution Data Taskforce met via Citrix GoTo teleconference on 03/12/2020 to discuss the following agenda items:

1. Discussion of Attribute Rating Scales

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

1. Discussion of Attribute Rating Scales

The Taskforce met for the first time on March 11, 2020, to discuss attribute rating scales for the Continuous Distribution of Lungs project. On this call, the Taskforce continued work on the post-transplant survival rating scale with discussions on factors that interact with cold ischemia time; approaches for estimating cold ischemia time; and use of straight-line distance versus travel distance.

Summary of discussion:

Factors that Interact with Cold Ischemia Time

UNOS staff asked the Taskforce to hypothesize donor characteristics that might have an interaction with cold ischemia time for SRTR to evaluate. Examples of donor characteristics that could have interactions with cold ischemia time include type of donor (DCD–Donation after Cardiac Death versus DBD–Donation after Brain Death) or age of donor (younger versus older).

A member suggested that SRTR evaluate the outcomes of extended criteria donor (ECD) lungs transplanted in high-risk recipients to see if there are certain factors that tend to lead to poorer outcomes, rather than trying to point to individual criteria like DCD. The member said that medical literature should have some starting points for defining ECD. The Vice Chair expressed concern that there is not enough data available, as many of the factors that define ECD lungs (like pulmonary consolidation) are not data points that are recorded in DonorNet, and the relationship between cold ischemia time and outcome varies widely in published literature. The Vice Chair suggested that SRTR evaluate some ECD criteria for an impact on post-transplant survival, particularly for certain recipients, to see if they have worse outcomes with ECD lungs.

UNOS staff asked the Taskforce about particular concerns for using DCD donor data, which led the Taskforce into a discussion of the possible impact of using DCD donors on post-transplant survival.

DCD Donors and Post-Transplant Survival

The Taskforce discussed concerns about factoring DCD donor type, particularly cases using ex vivo lung perfusion (EVLP), into modeling for post-transplant survival. The Vice Chair was not sure that enough data is captured to enable accurate evaluation of any differences. UNOS staff noted that SRTR would probably evaluate total ischemia time, particularly associated with travel and distance. The Vice Chair

said that there is a big difference between a donor who expires at 5 minutes versus a donor who expires at 29.5 minutes and that SRTR will not have the data to be able to capture this difference.

Another member expressed concern that incorporating these components into an allocation model now would not be based on reliable data; that it could limit access to donors for certain candidates; and that it would remove some decisions from the clinical judgement of transplant centers. The member noted that every donor and recipient match involves selection bias as the transplant team offsets risk factors with other favorable factors. The member noted that transplant centers are already held accountable for their outcomes at a pretty high level, which perhaps makes them less willing to consider higher-risk donors. The member noted that outcome data on DCD donors is limited, particularly since some of these lungs are discarded based on outcome on EVLP, and that the Taskforce should be careful about adding these factors to the allocation score if they are not confident in their reliability. Another member agreed, noting that the community began transplanting from DCD donors in 2009 and have achieved equivalent outcomes to DBD donors if not better without EVLP, suggesting that it is too premature to incorporate EVLP outcomes into the post-transplant survival model. Another member agreed that the Taskforce should be cautious about evaluating donor characteristics and the likelihood of a good outcome, particularly if it is not known whether EVLP was used on the donor lungs.

UNOS staff acknowledged the concerns about data reliability, sample size, and selection bias, noting that these concerns may justify using a simpler approach for now but that these factors could be revisited in the future when more information is available. The Vice Chair said that community members have expressed interest in this topic and may feel some frustration if it is not considered in the continuous distribution project, though the data may prove inadequate to include these factors in the composite allocation score. The Vice Chair asked about the possibility of looking at the data so that the results can be shared in the policy proposal, which might clarify if there is more of an opportunity to revisit this in the future, perhaps by collecting more information. SRTR staff agreed to evaluate a constrained list of donor criteria for their overall effect on post-transplant survival.

Interactions with Cold Ischemia Time

The Taskforce discussed donor age as a potential criterion to assess for interactions with cold ischemia time. A member noted that the International Society for Heart and Lung Transplantation (ISHLT) has explored this topic before, and another member mentioned a 1999 paper from Pittsburgh finding that old donor age combined with prolonged ischemic time showed significant risk. The Taskforce expressed support for evaluating the interaction between younger versus older donors and ischemia time and noted that medical literature can guide appropriate cutoff points for donor ages considered to be higher risk. HRSA staff agreed that it makes sense to evaluate this interaction since organs may also be traveling farther under a continuous distribution framework.

A member noted that recipient factors also impact clinical decision-making regarding donor age and accepting organ offers. UNOS staff acknowledged that selection bias is always a problem in this type of analyses, but noted that the model will be risk-adjusted in some sense because other factors from the LAS will be included in the modeling.

UNOS staff noted that since the current prevailing method for transporting and preserving lungs is not EVLP, UNOS and SRTR staff thought this criterion might be excluded from the model for now, but this could be revisited in the future if EVLP becomes more common. While one member agreed with this approach, another member said it would be helpful to know the impact of this interaction on the modeling because if its impact is relatively small, then including it in the model satisfies the concerns of the community without creating the previously discussed concerns about the impact on allocation. Overall, the Taskforce agreed to exclude the small number of EVLP cases from the modeling.

Estimating Cold Ischemia Time

SRTR staff led a discussion about using distance to estimate cold ischemia time, since ischemia time is not known at the time of the match run. SRTR staff shared a scatterplot showing that there is a lot of variability between straight-line distance and ischemia time, particularly at low distances. SRTR staff noted that past 500 nautical miles (nm), the relationship is largely linear. SRTR staff said that they will provide some sort of estimate of ischemia time as a function of distance but the interaction will not be clean because there are a lot of other unknown variables that influence ischemia time besides travel. SRTR will extrapolate this line out to the limit of the match run, which is 4,000 – 6,000 nm.

HRSA staff and Taskforce members discussed that there is an upper limit of ischemia time that surgeons keep in mind while considering logistical factors at the local level like operating room availability, surgeon availability, getting the recipient into the hospital, and other factors that can cause variability. When more travel time is involved, the variability of these other factors is mitigated to ensure the overall ischemia time stays below that upper limit. Given all of these factors, a member expressed surprise that there is any relationship between distance and ischemia time. SRTR staff noted that the correlation coefficient is not very high as only about 20% of the relationship is explained by the coefficient, but SRTR does not have a better proxy to estimate ischemia time.

A member said that the Taskforce should give people the benefit of the doubt in estimating the impact of ischemia time and that SRTR could simplify the process by incorporating the travel time based on mileage and the average implantation time into the model. SRTR staff explained that rather than estimate travel time and then estimate cold time separately, they would prefer to use straight-line distance to estimate cold time because straight-line distance is very highly correlated with travel time. SRTR staff noted that previous data requests have shown that straight-line distance does not have an association with post-transplant outcomes, which is probably not tolerable to the community and probably not realistic. The proposed framework is using straight-line distance to estimate total ischemia time with all the acknowledged shortcomings because total ischemia time does have a relationship with outcomes, so that would have a limiting effect on broader sharing based on post-transplant outcomes. A member responded that this approach would lead SRTR to always underestimate total ischemia time. SRTR staff responded that there would be some sort of representation of the variability in the scatterplot, possibly accounting for the transition between driving organs and flying organs.

Members expressed concern about this approach. SRTR staff explained that the idea is to account for the marginal increase in total ischemia time and its effect on post-transplant outcomes when sharing to a recipient that is 2,000 nm away compared to a recipient that is 0 nm away from the transplant center. A member expressed concern that the data points at 2,000 nm are influencing the overall slope of the line whereas if SRTR only looked at the relationship among the data points out to 1,000 nm, there would likely not be much of a relationship. SRTR staff noted that the data request will clarify how these lines are estimated and will estimate separate lines among various sharing distances.

A member noted that within 500 nm, the total ischemia time varies from 2 hours to 8 hours, so there is a lot of variability at short distances, and a recent UNOS study showed no impact on post-transplant survival based on ischemia time. The Vice Chair responded that looking at past data may not be that revealing because centers are making judgment calls about whether or not to accept certain donors if they are looking at longer total ischemia times. The member expressed concern about using data that is not robust to guide decisions impacting access for patients. The Vice Chair expressed concern about saying that ischemia time does not matter in the composite allocation score because clinicians know that it has an impact and take it into account when deciding whether or not to accept a certain donor. Forcing ischemia time into the model is not a great option but it has to be considered in some capacity. The member agreed that ischemia time matters but said it is not clear in what context it matters.

A member noted that it will be difficult to use cold ischemic time as a simple factor to estimate long-term outcomes, and suggested that the first step is to identify other interacting factors that indicate that patients will not do well with long ischemia time. The member suggested doing this analysis first and then determine if there is a way to use that interaction with cold ischemia time in the post-transplant survival model.

HRSA staff suggested updating the scatterplot to reflect donor age at shorter distances to see if any patterns emerge. SRTR staff agreed to evaluate whether there are other factors which are more predictive of ischemia time at shorter distances. A member noted that it could be something as simple as post-operative ECMO use that reduces the incidence of post-operative injury and offsets longer ischemia time. A member agreed that the question they need to answer is if total ischemia time and straight-line distance correlate better when other factors are added to the equation. SRTR staff were not confident that introducing other factors would clarify the relationship as their understanding is that a lot of the variability is behavioral, and SRTR does not have data on specific behavioral factors.

Straight-line Distance vs. Travel Distance

SRTR staff asked the Taskforce to consider whether modeling should use straight-line distance or travel distance. Straight-line distance measures the distance between two points whereas travel distance is computed based on a Google application programming interface (API) that accounts for infrastructure and geography. While there are some cases where straight-line distance and travel distance diverge, they are very highly correlated and it is easier from a modeling standpoint to use straight-line distance. Travel distance requires a lot of external resources whereas straight-line distance is a simple equation. SRTR staff noted that even for somewhere like Seattle where there is unusual geography, there generally is not a lot competition with other transplant centers, so it does not impact which transplant center has priority in terms of distance. That might not be true for all organs, but since lung transplant centers are not as common, candidates at these centers would not be disadvantaged. SRTR staff said that they would be able to demonstrate these cases for a policy proposal.

UNOS staff expressed support for straight-line distance because it is known, transparent, stable, and has been shown not to disadvantage lung candidates, whereas using travel distance is more complicated and does not necessarily yield better results. UNOS staff explained that in order to use travel distance, the OPTN would need to recreate the Google API and make the database publicly available. UNOS staff noted that travel distance changes as infrastructure changes whereas straight-line distance stays constant.

Next steps:

The Taskforce will meet again on April 9, 2020, to continue the discussion on which donors SRTR should evaluate for interactions with cold ischemia time, like extended criteria donors or older age donors.

Upcoming Meetings

- April 9, 2020 (Taskforce)
- April 16, 2020 (Workgroup)