

**OPTN/UNOS Thoracic Organ Transplantation Committee
Meeting Minutes
October 5, 2017
Chicago, IL**

**Kevin Chan, MD, Chair
Ryan Davies, MD, Vice Chair**

Introduction

The Thoracic Committee met via Citrix GoToTraining teleconference in Chicago, IL on 10/05/2017 to discuss the following agenda items:

1. Committee Project Portfolio - Action Items
2. Fall 2017 Public Comment Review
3. Committee Project Portfolio - Monitoring Updates
4. Other Significant Items

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

1. Committee Project Portfolio – Action Items

Summary of discussion:

- a. Regional Review Board Guidance for Adult Congenital Heart Disease Exception Requests

The Committee reviewed public comment feedback. The comments were submitted by multiple different types of commenters: 11 regions, 2 committees and 5 societies. The proposal was on the non-discussion agenda and passed in all regions. The only meeting where there was any discussion was in the Region 5 breakout. Per the regional rep, the breakout attendees had no questions or comments other than that they thought the guidance document appropriately addressed the original concerns that were expressed during the fall 2016 Region 5 meeting regarding how this population was stratified in the adult heart allocation proposal. Both the Pediatrics and Patient Affairs Committee heard the proposal and supported unanimously. In addition, five societies commented and generally supported the proposal. Being a relatively non-controversial guidance document, the proposal did not receive many comments. The identified themes were primarily formed by OPTN Committee and society feedback:

1. Nature of guidance
2. Exception requests
3. National specialty or pediatric review board
4. Further stratification of ACHD subgroups

In addition, the proposal garnered a few single comments the Committee evaluated and will respond to in the Board of Directors briefing paper.

Nature of Guidance

A chief concern was the nature or interpretation of guidance generally:

- Limitations of guidance (versus policy)
- Interpretation of guidance de facto policy

On one end of the spectrum, commenters noted the limitations of guidance as voluntary and not enforceable. If utilization is voluntary, commenters questioned whether review boards

would use it. If they do not use it, how does this effectively address transplant community's initial concerns? The Committee noted that OPTN-developed guidance tended to be readily adopted by the thoracic community; for example, the guidance developed for status 1A device complications helped standardize the award of exception requests for those conditions and ultimately was incorporated into the new adult heart allocation policy. In addition, apart from actually changing policy, the community asked for further guidance to how these candidates might access higher urgency statuses. Other commenters were concerned that review boards would interpret this guidance as de facto policy, as there is such a high uptake of guidance by the thoracic community. Should review boards interpret the guidelines as stringently as policy, would that negatively impact ACHD candidates applying for exceptions who don't meet the criteria the Committee outlined? The Committee felt that the dedicated education review boards would receive during implementation of the adult heart allocation policy changes would be the best opportunity to reinforce the guidance were merely recommendations, and review boards could always grant exceptions to candidates seeking access to higher statuses who do not meet the suggested criteria. As long as the review board agrees that the transplant program has provided compelling evidence that their candidate has an urgency and potential for benefit comparable to that of other candidates at the requested status, it is within their purview to grant (or deny) any exception. Ultimately, the Committee agreed to respond to these concerns via the Board briefing paper, but not modify the guidance.

Exception requests

Another prevalent theme was around CHD exception requests generally:

- Increase in exception requests
- Data collection around exception requests

There were several comments about whether this guidance (or more likely, the implementation of the adult heart allocation policy changes itself) could have unintended consequences and lead to an increase in exception requests for this patient population. Members noted that the need for exceptions would be a smaller subset of the overall adult CHD group; every adult CHD candidate should not require an exception. The STS and ASTS advised robust data collection to determine the frequency of the exception requests and acceptances, in addition to the waitlist mortality to monitor program behavior. The Committee discussed this feedback. While there could possibly be a bolus effect with exceptions as the community really gets familiar with the adult heart allocation policy (as seen with the pediatric heart policy changes), members acknowledged that the Committee cannot predict at this time whether that hypothetical situation would persist. Members did not feel the guidance in and of itself would cause an increase in exceptions. The Committee confirmed it will track exception data as part of the monitoring plan, but that information may also inform other future projects, such as a national review board. The Committee agreed to respond to these concerns via the Board briefing paper, but not modify the guidance.

National specialty or pediatric review board

Several commenters called for the Committee to consider a national pediatric or specialty (CHD) review board. Such a board may resolve the problem in the variability in the evaluation and award of exception requests for adult congenital heart disease candidates region to region due to limited or inconsistent congenital heart disease or general pediatric expertise on regional review boards. While the Committee strongly supported this suggestion, it acknowledged that such a change was clearly beyond the scope of this proposal. It is the Committee's intent to pursue such a project (a national heart review board) in the near future. This board could include specialty boards for specific diagnoses or

pediatrics, similar to the national liver review board. Ultimately, the Committee agreed to respond to these concerns via the Board briefing paper, but not modify the guidance.

Further stratification of ACHD subgroups

Finally, several societies critiqued the fact the guidance failed to stratify the ACHD patient population more granularly into subgroups with higher risk. International Society of Heart and Lung Transplantation (ISHLT) commented that the guidance failed to capture the complexities of risk assessment in this patient population. The Vice Chair shared the Committee grappled with this very subject while developing the adult heart allocation policy, and similarly, the workgroup didn't feel they could get much more specific based on the data that is currently available, even smaller, single-center studies. The Committee considered keeping the guidance as proposed during public comment or attempting to further stratify this population by waitlist mortality. The Committee noted no suggestions on how to further categorize this population were offered, and there was some concern that could lead to substantive changes. The Committee agreed to respond to these concerns via the Board briefing paper, but not modify the guidance.

Although not identified as a theme, there was a comment from ISHLT that there seemed to be an emphasis placed on treatment decisions that are subjective (i.e., the decision to treat a patient in the hospital vs. as an outpatient and the decision to start a patient on inotropes). The Committee confirmed that hospitalization is required for all status 1-3 exceptions, and a policy change to alter that is beyond the scope of this project. They also raised concerns that the proposed requirements for specific inotropes and dosages for status 2 exceptions for single ventricle ACHD candidates are arbitrary for this group, and it is possible that they may not benefit and may even potentially be harmed by the use of high-dose inotropes. In an early draft submitted to the Heart Subcommittee, inotropes were included as criteria, but dosages not specified. The Subcommittee had recommended including the specific dosages from the adult heart allocation policy as a matter of consistency, and to mitigate concerns around gaming, especially as the guidance does not require continuous hemodynamic monitoring via pulmonary artery catheter or other invasive device. The Committee debated whether to tweak or remove the inotrope dosages, or keep the guidance as proposed during public comment. Members did not suggest modifying the inotrope dosages, but advised adding an "or" caveat to the effect of requiring evidence of intolerance to maximally-tolerated inotropic dosages. The Committee agreed to add this verbiage to both the single and dual ventricle criteria.

There was consensus to define ventricular assist device (VAD) complications, as referenced in the status 1 exception criteria for single ventricle candidates. It was not the Committee's intent for VAD complications to include such diagnoses as driveline cellulitis. The Committee agreed that for consistency, VAD complications would be limited to those specified in the new policy.

The Committee voted unanimously (16-yes, 0-no, 0-abstentions) to approve the guidance with the minor modifications specified and send to the Board of Directors for consideration. It was noted this guidance will not be utilized by review boards until the adult heart allocation policy changes are fully implemented.

b. Hypertrophic Cardiomyopathy/Restrictive Cardiomyopathy Exception Request Guidance for Review Boards

The Committee reviewed revised criteria (Appendix A) most recently informed by the Heart Subcommittee's feedback during their September meeting. Therefore, generally, the revised criteria is more prescriptive and specific, and to the extent possible, the lab values and

hemodynamic parameters align with the approved adult heart allocation system policy language. In addition, as was noted in the adult congenital heart disease guidance, candidates must be hospitalized and present with a specific diagnosis (Class IV heart failure).

The Committee considered the status 2 criteria. Unlike the adult congenital disease population, hypertrophic and restrictive cardiomyopathies are hemodynamic-driven diagnoses. Therefore, the criteria recommends the candidate has a pulmonary artery catheter to be eligible for a status 2 exception. Inotropic therapies are not typically appropriate or useful in these populations, which is one reason specific dosages will not be included in the criteria. Rather, the criteria includes specific parameters that indicate hemodynamic instability, poor perfusion or end-organ dysfunction, despite the patient being on maximally-tolerated inotropes. The criteria also notes that a weaning attempt (off inotropes) would not be required for these candidates before a program would file for an extension (which is reviewed retrospectively by a review board). This requirement would be waived because it may jeopardize these patients, who are not candidates for mechanical circulatory support devices.

The Committee moved on to discussing status 3 criteria. The differences between this criteria and the criteria for a status 2 exception is the cardiac index ($CI < 1.8$ vs. ≤ 2.2) and prior to inotrope administration, the candidate shows evidence of decompensated heart failure and poor perfusion, versus meeting the parameters while currently on maximally-tolerated inotropes. In addition, there is no non-invasive hemodynamic monitoring option recommended as an alternative for a status 2 exception criteria. One member suggested including a monitoring option that captures cardiac output and left ventricular filling pressures rather than requiring an invasive monitor, however, several Committee members felt that the invasive monitoring requirement was reasonable for a status 2 exception, which would have access to broader sharing.

The Committee debated whether or not to include the specific inotrope dosages included in adult heart policy, but did not feel strongly about including. Members thought it was unrealistic to recommend those target doses because these candidates cannot tolerate them. The Heart Subcommittee confirmed this was a primary concern for the workgroup.

The cardiogenic shock requirements are less stringent in guidance than the approved policy, which requires a candidate meet all of the sub-criteria within one 24 hour period. For this patient population, the systolic blood pressure requirement may be challenging to meet. Therefore, the guidance recommends the candidate meet two of a list of hemodynamic and end-organ dysfunction indicators. The Committee felt comfortable with this recommendation.

Some members expressed concern about being overly prescriptive and losing sight that these are guidelines, not policy. The Committee acknowledged balancing including enough specificity that the guidance is useful for review board members but not so prescriptive that review boards member decline exception requests that don't align exactly with the recommendations.

The only other substantive comments the Committee made was to note this guidance should not apply to patients with dilated cardiomyopathy who are candidates for mechanical support.

- c. Modifications of the lung transplant follow-up form (TRF) to better characterize longitudinal change in lung function following transplantation

The Committee was informed the project name was modified from "Modification of the Lung Transplant Follow-up Form (TRF) to Include CLAD Data" to the current name to better

reflect the goal of the changes. There were no objections from Committee members. The following data elements were presented to the Committee for feedback:

- FEV1
- FVC
- FEF25-75

The Subcommittee felt these data elements were objective, readily available to coordinators, and relevant to current chronic lung dysfunction definitions. Collecting these elements at three time intervals was a compromise the Subcommittee was comfortable with, but welcomed feedback from the full Committee. The Subcommittee proposes collecting these data on the 6-month, 1-5 year and 6+ year TRF, acknowledging that the further out a patient is from transplant, the less often they get testing done, therefore, the less complete or useful the data might potentially be.

Members felt strongly that the time intervals should be defined before sending the proposal out for public comment. Suggestions included every other month or quarterly. UNOS staff assured the Committee that validation was in place to restrict the timeframe to some degree. One member asked how a program would report data for a patient who did two PFTs within the proposed timeframe, but not a total of three. UNOS staff explained that the “status” drop-down (missing, unknown, N/A or not done) would cover this scenario. Conversely, this “out” also may limit the utility of the data, if programs report this status instead of actual values.

A new Committee member asked how the peak pulmonary function test (PFT) results would be captured. The Lung Subcommittee Chair explained the Subcommittee debated asking for peak PFT results, but felt that the result would be biased if just the best results were reported. Asking for results across several time intervals should capture peak results, but perhaps not on an individual level.

The Committee discussed whether to modify or remove the “bronchial stricture” and the oxygen at rest questions. While these data elements don’t directly contribute to the lung allocation score (LAS), they can help identify risk factors that do inform the LAS. There was some debate on whether to just capture stenosis on the 6-month form, not capture it at all, or capture it for a limited time beyond 6-months (1 or 2 years). When evaluating for chronic lung rejection, ruling out presence of bronchial stricture is required. One member mentioned ISHLT might be examining stenosis more critically to better define and report it. The group acknowledged that multiple factors could impact strictures: the surgery itself, Ex-vivo lung perfusion (EVLP), recipient factors, etc. While it may not impact survival, it does interplay with quality of life and lung function. The Committee agreed that the way the bronchial stricture questions was asked likely contributed to the inability to interpret the data and the question in its current form should be eliminated. The group could not come to consensus on how to reword the question, and agreed to ask the community this question during public comment. In order for the information to be more useful, it needs to be more granular. There was consensus to keep the oxygen requirement at rest because it is important in survival analysis. The Subcommittee determined the question would be expanded to also capture oxygen requirement with exercise.

2. 2017 Fall Public Comment Review

The Committee reviewed selected proposals out for public comment and provided feedback to the sponsoring committees.

Summary of discussion:

a. System Optimizations to Expedite Organ Allocation and Increase Utilization – OPO Committee

The Committee commends the OPO Committee's efforts to increase the number by improving the placement of organs and potentially reducing organ discards, leading to an overall increase in the number of transplants. The Committee shared several concerns. First, subsequent testing, donor hemodynamics or other offers could impact a program's decision to accept an organ, and having to accept earlier (well before an established OR time) may lead to an increase in late back-outs. Another area for concern was around the required versus optional donor information. As part of this proposal, the requested (optional) donor information was removed and the (required) donor information was heavily edited. Some felt that it was pared down too much, and tests such as a bronchoscopy for lung or cardiac catheterization or inotrope dosages, (i.e. information almost universally preferred) are missing from policy. There was a suggestion that the OPO document the reason why a test, if performed (such as a bronchoscopy) cannot be done. It was noted that not having this information preferred but not required information may potentially delay some programs from accepting an organ. The Committee recommended an expanded, rather than limited, required donor information list. The Committee noted that highly-sensitized thoracic candidates were a special population that may be negatively impacted by this proposal, based on the way thoracic organs are offered to this group. One Committee member pointed out that data on how many organs are discarded or lost by delays in offers, acceptance and placement should be included. Another member shared concerns that in situations where potential donor information is taken by a 3rd-party OPO consult service, information sometimes get further delayed or critical information missing. This operational staffing process has implications for this project (further delays information-sharing). Finally, there was some consensus for to amend the time limit to responding to electronic organ offers: a total of 60 minutes was palatable, rather than the more stringent 30/30 policy proposal.

b. Revisions to Pediatric Emergency Membership Exception – Pediatrics Committee

The Committee commends the Pediatrics Committee's efforts to ensure safety and outcomes in pediatric transplant recipients by clarifying when a transplant program that is not otherwise approved to perform pediatric transplants can perform an emergency transplant into a pediatric heart candidate. The Committee felt that the requirement for a consult with a transplant program with an approved pediatric heart component confirming that it is not medically advisable to transport the patient to an approved pediatric heart transplant program was reasonable, but that it was somewhat arbitrary to limit this particular criteria to candidates on extra-corporeal membrane oxygenation (ECMO) or with a non-dischargeable VAD. There was concern that a pediatric candidate might not be transportable for other reasons (other-wise medically urgent, unstable or geographically isolated, etc.) and therefore the pathway should not be limited to just those status 1A candidates on ECMO or a non-dischargeable VAD. The Committee supported the provisions outlining that contingent upon a consult with a transplant program with an approved pediatric heart component, documentation that it is not medically advisable to transport any medically urgent candidate (those candidates who meet policy requirements outlined in OPTN Policy 6.2.A: Pediatric Heart Status 1A Requirements) was sufficient, and that the pathway should not be limited to those candidates that cannot be transported due to being supported by ECMO or a non-dischargeable VAD.

3. Committee Project Portfolio - Monitoring Updates

Data Summary:

a. Modifications to Pediatric Heart Allocation

The Committee received a regular monitoring update on the policy changes to the pediatric heart policy changes, implemented in 2016.

Data showed a continued trend around increased exceptions. There was also an increase in the number of transplants generally and more 1A (by exception) recipients with cardiomyopathy being transplanted. There were fewer 1A additions to the waiting list overall. There was an increase in ABO incompatible transplants to recipients under the age of 1 year and no change in ABO incompatible transplants to recipients 1-2 years of age after titer change.

UNOS staff asked if there could be some other potential explanation to the increase in status 1A exceptions, beyond the policy changes. Transplant by exception seem to be benefitting a particular group of candidates, which may be negatively impacting other groups. The Committee noted that the increase in exceptions generally runs contradictory to one of the goals of the project, which was to reduce the number of exceptions for status 1A. One Committee member asked if the initial 6 months post-policy implementation was compared to the most recent 6-month era to see whether candidates who previously qualified as status 1A but no longer do under the revised policy were the ones driving the exceptions, and if that has persisted.

A UNOS staff member asked whether programs were reporting cardiomyopathy as an “other” congenital heart disease diagnosis, when that was not the intent. UNOS staff advised they would explore that further.

b. LAS Revision

The Committee received a limited monitoring report comparing LAS pre- and post-implementation by diagnosis group, death and transplant rates for candidates, and recipient survival. Data showed match LAS at listing changed significantly; there was an increase for group B and a decrease for group D. There was a significant change in ranks within the diagnosis groups. Data showed a decrease in deaths per 100 patient years while waiting and an increase in transplants per 100 active patient years while waiting. In addition, data revealed an increase in the number of lung transplants across the majority of regions. Finally, there was a significant increase in survival rates.

The Committee also noted that mean LAS at transplant decreased across almost all regions. There is still variability in LAS across regions, ranging from 45-65 in the cohort analyzed. Some variability may be due to the volume of lung transplants done within the region, what diagnosis groups are ultimately transplanted and program listing practices. Members found this data might be informative as the Lung Subcommittee continue to consider a broader geographic sharing of adult lungs project.

c. EVLP Data Collection

UNOS staff presented an update to the Committee regarding data reported based on the fields added to the deceased donor registration form (DDR) in 2015. The majority of lungs recovered for transplant did not have machine perfusion intended or performed prior to transplant. A total of 254 donor lungs had machine perfusion intended or performed prior to transplant. Of lungs that indicated machine perfusion intended or performed prior to transplant, if one lung was perfused, typically the second lung was also perfused. Approximately half of the lungs with machine perfusion intended or

performed prior to transplant were transplanted. Additional data to be collected on transplant recipient registration form. Members commented that the most stunning revelation was that 5% of recovered lungs were ultimately discarded-this does not align with procurement practices (recovered lungs are rarely discarded). UNOS staff responded that this result was likely due to variability in reporting. Several members commented that variability in number of OPO's reporting intent to perfuse lungs may be artificial, as the Donation Service Areas (DSA's) with the highest volumes of lungs with machine perfusion prior to transplant were those that included transplant programs enrolled in various EVLP clinical trials.

d. Pediatric Lung Allocation Policy Changes

UNOS staff presented three month post-implementation data to the Committee. While the sample size is still small, it can be seen that pediatric lungs are being transplanted in pediatric recipients in distances as far as Zone B. As the cohort of pediatric donors increases over time, the broader sharing of pediatric lungs to pediatric recipients should become more apparent. Pediatric donor lungs are being allocated to pediatric candidates first per policy. So far, only 1 candidate under 2 years old has indicated they are willing to receive an ABO incompatible lung and no ABO incompatible lung transplants have been performed for candidates under 2 years old. However, this sample size and population is small and will be continued to be monitored. Committee members had no questions.

4. Other Significant Items

a. Scientific Registry of Transplant Recipients (SRTR) Organ Acceptance Modeling Update

The SRTR contract with HRSA states the Program Specific Reports (PSR) shall include information on organ acceptance. In June 2017, the SRTR solicited feedback from both the Lung and Heart Subcommittees to inform the thoracic organ acceptance models. SRTR reported the models to the Committee prior to implementation.

Several members were concerned that the acceptance criteria was not granular enough, or incomplete. There were additional concerns pertaining to the optics around how the metrics are presented to the public, which, in their opinion, seemed to be how likely the program is to accept an offer. There was general concern that there was not sufficient plain language direction or guidance for patients to enable understanding of the information on the SRTR website. They felt the model's pre-acceptance criteria was too narrow. The model doesn't take into account certain variables that may cause a program to defer on an organ when initially offered (e.g. listed unacceptable antigens) versus a program actually turning down an offer (e.g. post positive crossmatch). There was also concern that the turn-down rate would be skewed if a program has the first several candidates on the match run and turns down the organ for all but the last candidate listed at their center.

Upcoming Meeting

- November, 2017

APPENDIX A: DRAFT HCM/RCM Exception Request Criteria

The criteria described herein is appropriate for the following categories of candidates:

- HCM diagnosis based on 2011 ACCF/AHA Diagnostic Criteria
- Primary restrictive cardiomyopathy, of idiopathic or genetic origin, or secondary to radiation
- Infiltrative cardiomyopathy (e.g. cardiac amyloidosis (TTR or AL), based on AHA criteria/ISHLT guidelines (2006, 2016)).

Review boards should use caution in applying these criteria (intended for candidates with restricted ventricular chamber size and poor candidacy for ventricular assist devices) to patients with a primary diagnosis of HCM, with a dilated LV. The criteria are not intended to apply to patients with restrictive physiology based on other primary diseases. Therefore, coronary artery disease or transplant coronary artery vasculopathy or chronic rejection, for example, do not fall under this guidance. In such patients, who do not otherwise clearly have a contraindication to durable or temporary support therapies, review boards should consider that they may not be higher risk for mechanical support or other therapies than patients with DCM.

It is important to note that in all cases, candidates must be admitted to the transplant hospital that registered the candidate on the waiting list to be eligible for exceptions to status 1-3.

Most candidates, in the absence of the conditions below, are appropriately categorized in status 4. Table 1 provides useful guidance for RRBs asked to approve upgraded listing urgency by exception for hypertrophic, primary or infiltrative or radiation-induced restrictive cardiomyopathy.

Table 1: Guidance for RRBs

| If the candidate meets this criteria: | Then the candidate is eligible for: |
|--|-------------------------------------|
| <p>Is admitted to the transplant hospital that registered the candidate on the waiting list, has NYHA class IV heart failure symptoms, and is <u>experiencing all of the following</u>:</p> <ul style="list-style-type: none"> • Continuous monitoring of hemodynamic data, including cardiac output, with a pulmonary artery catheter • Has reached maximally-tolerated inotropic doses (as evidenced by unstable atrial or ventricular arrhythmias, or worsening of an intra-cavitary gradient) and <u>continues to have at least 2 of the following</u>: <ul style="list-style-type: none"> ○ Systolic blood pressure < 90 mmHg ○ Sustained elevation in filling pressures LA or RA or LV or RVEDP or PCWP > 15 mmHg ○ Persistently low CI ≤ 2.2 L/min/m² ○ SvO₂ < 50% ○ Elevated arterial lactate to 2.5 mmol/L ○ Increase in serum creatinine > 20% above baseline ○ Increase in total bilirubin > 20% above baseline ○ AST or ALT > 2x upper limit of normal • If the exception is granted, the Status remains valid until transplant. | <p>Status 2 exception</p> |

| If the candidate meets this criteria: | Then the candidate is eligible for: |
|--|-------------------------------------|
| <p>Is admitted to the transplant hospital that registered the candidate on the waiting list and meets <i>all</i> of the following criteria:</p> <ul style="list-style-type: none"> • Has <i>one</i> of the following: <ul style="list-style-type: none"> ○ Invasive pulmonary artery catheter ○ Daily hemodynamic monitoring to measure cardiac output and left ventricular filling pressures • Is supported by continuous inotropic infusion to improve end-organ perfusion/function • Prior to initiation of inotropes, the patient demonstrated evidence of decompensated heart failure, as evidenced by <i>at least two</i> of the following: <ul style="list-style-type: none"> ○ Systolic blood pressure < 90 mmHg ○ LA or RA or LV or RVEDP or PCWP > 15 mmHg ○ Cardiac index < 1.8 L/min ○ Elevated arterial lactate to 2.5 mmol/L ○ Increase in serum creatinine > 20% above baseline ○ Increase in total bilirubin > 20% above baseline ○ AST or ALT > 2x upper limit of normal • If the exception is granted, the Status remains valid until transplant. | <p>Status 3 exception</p> |