OPTN Heart Committee
Meeting Summary
August 15, 2023
Conference Call

Richard Daly, MD, Chair
Jondavid Menteer, MD, Vice Chair

Introduction

The Heart Committee met via Webex teleconference on 08/15/2023 to discuss the following agenda items:

1. Public comment: OPTN Ethics Committee: Ethical Analysis of Normothermic Regional Perfusion
2. Public comment and regional meeting feedback addressing the policy proposal and concept paper
3. Additional considerations within pediatric medical urgency attribute
4. Reminder of 09/22 in-person meeting and closing remarks

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

1. Public comment: OPTN Ethics Committee: Ethical Analysis of Normothermic Regional Perfusion

The members of the OPTN Heart Transplantation Committee members and the OPTN Ethics Committee Chair had a robust discussion about the Ethics Committee's white paper, Ethical Analysis of Normothermic Regional Perfusion (NRP). A Heart Committee member had participated in the workgroup created by the Ethics Committee to address the topic.

Discussion Summary

The Chair of the OPTN Ethics Committee presented the white paper to the Heart Committee members. The Ethics Committee Chair began the presentation by explaining that the presentation involves four major components: a brief review of the relevance of the Uniform Declaration of Death Act (UDDA); an overview of the uniqueness of NRP to organ procurement; Discuss details of the Ethics Committee's analysis and conclusions; and then share important reminders that the Ethics Committee's general approach to writing white papers is that they be analysis-based, not justification-based.

The Ethics Committee Chair told the Committee members that the UDDA, which is an important legal framework and highly relevant for the Ethics Committee's ethical analysis, is currently being re-litigated. However, it is beyond the scope of the white paper to speculate about what future iterations of the UDDA may contain. For purposes of their analysis, the Ethics Committee treats the UDDA with authority.

NRP is unique because, unlike other machine perfusion techniques, it relies on the restoration of circulation regionally in the donor body before the organs are removed and after circulatory death is declared on the basis of permanent cessation of circulation. This is important because it differs from standard DCD, in which, no blood circulation occurs after death is declared by circulatory criteria when restoration of circulation occurs with NRP, ligation of vessels and other methods cand be used to prevent circulation from reaching the brain. This is a crucial difference between NRP and other forms of organ procurement.

The Ethics Committee Chair pointed out that they had adopted a procedural justice approach to the analysis, which involved engaging diverse stakeholders, as well as a collaborative, transparent process. The workgroup created to work on the analysis consisted of individuals who, prior to starting the project, were partial to or skeptical of NRP as an ethical practice. The workgroup included transplant surgeons, ethicists, lawyers, OPO coordinators, and donor families. Other OPTN committees were represented on the workgroup. The workgroup undertook a comprehensive process in completing the analysis.

The white paper examines the ethical implications of NRP, according to the principles of non-maleficence, otherwise known as 'do no harm,' and 'respect for persons, often going by autonomy and utility. These principles, which are the bedrock of transplants ethics, are established in the OPTN white paper. Abiding by these ethical principles supports trust in the transplant system. The Ethics Committee seeks to balance these principles, which sometimes stand intention with one another, and considers each principle thoroughly in its analysis. Intent has come up a number of times in workgroup's discussion, and is currently being addressed under the principle of autonomy.

According to the Ethics Committee Chair, NRP has two main implications for non-maleficence. Most importantly, there is concern that NRP violates the dead donor rule. The dead donor rule states that donors must be dead at the time of organ procurement, and that donation must not cause death. The Ethics Committee adopted this definition because it is consistent with how the Committee has referred to the dead donor rule in the past.

The Ethics Committee Chair stated two main concerns about NRP involving maleficence. First, that after circulation has been restored, does the person continue to meet the criteria required for determination of death, even when no attempt is made to resuscitate. Donors are not assessed for neurological criteria, and therefore, cannot be said to meet brain death criteria at the time of donation. Second, more research is potentially needed to confirm that profusion of the brain and brainstem during NRP does not occur.

The Ethics Chair addressed the information that should be shared with a donor's family and/or caregivers, particularly how circulation is restored regionally, which can include the heart. Additional information should be provided that the donor has not been assessed to meet the criteria for brain death. The Ethics Chair also highlighted the workgroup's discussion of uncontrolled scenarios, in which circulation occurs unexpectedly. Such circumstances raise concerns about non-maleficence and respect for persons given the difficulty to achieve informed decision-making. The Ethics Committee members and the workgroup members determined that the concerns regarding non-maleficence and respect for persons do not justify performing uncontrolled scenarios.

According to the Ethics Committee Chair, the Committee and workgroup members conclude that NRP presents a promising and exciting technology which holds the potential to increase the number of transplantable organs and the quality of these organs. These represent worthy and important goals. As with all new technologies consideration for how the technology can be implemented ethically, is critical to its widespread adoption and acceptance by the public. The Chair continued that the Ethics Committee shares the enthusiasm of the transplant community in developing and implementing solutions to improve the transplant system and reduce wait times and deaths for patients awaiting organ transplantation. The committee also affirms the sacred trust and commitment of the transplant community to organ donors and donor families to maintain ethical and transparent donation procedures.

It is with these commitments and understandings that the committee concludes that the OPTN should proceed, but proceed cautiously regarding the practice of NRP for organ procurement. So, think yellow

light not red light or green light. The following items require consideration and resolution. First, an assurance that NRP adheres to the dead donor rule. Second, that non-maleficence must not be violated in pursuit of NRP despite positive utility outcomes. Third, the standardized and transparent protocols, including adequate informed decision-making with patients, pre-mortem or whatever we determine this happens to be and the families approached about donation, are necessary preconditions for any ethical pursuit of NRP. And, the Ethics Committee agreed that uncontrolled scenarios for any form of NRP should not be performed at this time because of the added concerns regarding non-maleficence and respect for persons. The Chair stated that the white paper is absolutely not a referendum on the clinicians, transplant centers, or OPOs who engage in NRP.

Heart Committee members thanked the Ethics Chair for that Committee's work on the white paper, and for the opportunity to comment. Heart Committee members who were familiar with the white paper's ethical analysis and/or the debate surrounding NRP expressed gratitude to the Ethics Committee for tackling the subject and producing a neutral analysis that at the same time raises important questions that need consideration. A Heart Committee member who served on the NRP workgroup summarized that through the white paper, the Ethics Committee is attempting to define the ethical positions within the current framework, of what the definition of death is.

Some Committee members questioned whether the Uniform Declaration of Death Act (UDDA) is still appropriate given the advances biological understanding that have occurred in the 50 years since the UDDA was released, and whether it the UDDA should be updated to reflect the new knowledge? The Ethics Committee Chair said that the ethical analysis in the white paper considers potential implications of NRP according to the UDDA as it currently stands. The Ethics Chair also told the Heart Committee that the UDDA is currently being reviewed by the Uniform Law Commission (ULC), and encouraged Heart Committee members to engage in ULC meetings if they see opportunities to improve the UDDA.

Committee members also asked if NRP violates the UDDA, to which the Ethics Committee Chair responded that the ethical analysis identifies serious concerns that it does violate even the weaker version of the dead donor rule. The Ethics Chair continued that the Ethics Committee is open to persuasion as to whether that alone should be the primary consideration in making a final determination. The Ethics Chair said they see this as a question for society.

A Heart Committee member pointed out that the white paper recommends that the transplant community "proceed cautiously" with regard to NRP. The members suggested that the Ethics Committee might want to consider clarifying what is meant by "proceed cautiously" and/or how the transplant community might interpret the phrase. The Ethics Chair responded that this has been a very frequently asked question about the white paper. The Ethics Committee has intentionally leaving the public with ambivalence around the question because it is really up to society to determine the extent to which society is comfortable living with potential infractions or lack of compatibility with the dead donor rule? It is even more challenging to answer the question because transplant centers already initiated NRP before the ethical analysis was done. The Ethics Chair reiterated that this is a values-based question. The Ethics Chair added that they plan on recommending that the Ethics Committee drop the reference to proceeding cautiously in favor of directing the public to think about what it wants to do.

Heart Committee members asked whether the decision to use NRP should be up to the individual transplant programs or OPOs, rather than addressed nationally? A member commented that what the analyses describes gets "in between" the patient-doctor relationship, and that can have negative consequences. It was suggested that perhaps the ethical analyses should be less prescriptive, and would be better framed as a societal question. Another member said that how the discussions about NRP are

handled between the donor families and caregivers and the transplant program staff is also critical. The discussions need to be very specific and very clear about the purposes, and associated benefits and risks that come with the procedure. Another member suggested that examining how the organ recipients are informed and involved with the whole process might also be beneficial.

Next Steps

Heart Committee members were encouraged to submit feedback about the white paper to the OPTN website. Contractor staff will draft a formal Committee response based on today's conversation and share it with Committee leadership for review and eventual submission to the OPTN website.

2. Public comment and regional meeting feedback addressing the policy proposal and concept paper

Contractor staff updated the Committee members on the latest public comment feedback received for the *Amend Adult Heart Status 2 Mechanical Device Requirements* policy proposal (Status 2) and the *Continuous Distribution of Heart* concept paper.

Discussion Summary

Committee members were updated on the public comments submitted to the OPTN website and the regional meeting feedback. Beginning with the Status 2 proposal, the regional meeting sentiment has largely been in support of the proposal, or neutral. Generally, there has been support for addressing the use of IABPs as a result of the increase in the volume of stats 2 candidates.

The bulk of feedback received has been associated with the timeframe a candidate must be receiving inotropic therapy to qualify for the status 2 criteria. The subcommittee developing the proposal chose not to be overly prescriptive in telling physicians when to start and stop therapy. Other concerns expressed by the community include the likelihood that exception requests will increase as a result of the proposed policy changes. Contractor staff said that as public comment gets closer to the end, that the Committee will be asked to review the policy proposal and determine what, if any, changes suggested in public comment or at the regional meetings should be made.

It was stated that the community has demonstrated that they want donor hearts first and foremost. There will likely be a desire to continue using this pathway to get candidates' greater priority to transplant. It was pointed out that the increased use of temporary MCSDs to attain a high priority status is a topic that is widely criticized by the community in general, but the Heart Committee's proposed solution is starting to receive criticism. It was also discussed that the regional review boards need to be better informed about the information needed to approve an exception request.

The Chair added that there has been feedback regarding how the proposal impacts the presence of arrythmias among patients. The Committee may want to consider creating a guidance document to help regional review board members address the likely increase in exception requests. The Chair stated that just demonstrating a history of arrythmias may not be sufficient to meet the Committee's intention with the proposed policy. A demonstration of arrythmia or on-going issues with arrythmias seems more appropriate given the Committee's efforts. Another member suggested that the Committee may need to identify what it means to fail inotropic therapy in terms of clinical conditions or values, such as intolerance of milrinone or a PAPi value.

A Committee member asked whether there are regional differences around the use of temporary mechanical supports that appear in terms of short transplant times.

It was also mentioned that the regional meeting presenter needs to push back and ask the attendees to describe why they think the status quo is better than what is being proposed, or how can the Committee address the issue differently?

Regarding the feedback about arrythmias, the subcommittee considered the topic during their deliberations and wanted to create a straightforward proposal that would not necessarily require a lot of programming in the OPTN Computer System. Along those lines, the subcommittee chose to move forward relying on existing policy criteria, rather than creating new criteria that would require substantial new data analysis and a longer timetable. Perhaps, the Committee could consider including more specific clinical values as part of a guidance document for the regional review boards.

Contractor staff provided a quick update on the feedback received for the continuous distribution concept paper. The public comments on the OPTN website have asked about the specifics the Committee intends to address with continuous distribution. From the regional meeting perspective, there have been recommendations for the Committee to consider new attributes, such as short stature candidates. The Chair stated that the idea of addressing short stature as an attribute had been raised by the Lung Committee, and others, but the Heart Committee in its previous deliberations determined that it has less application to heart allocation. A question about whether heart-lung allocation would be considered as a separate attribute also came from the Lung Committee. The Heart Committee members pointed out that the Multi-Organ Transplantation Committee will be addressing those topics.

Next Steps

The Contractor will continue updating the Committee members regarding public comments and regional feedback concerning the two projects.

3. Additional considerations within pediatric medical urgency attribute

The Committee may want to consider providing additional priority within the continuous distribution allocation framework for pediatric candidates who experience limited access to donor hearts because of their physical size and because of their somewhat stable, but high medical urgency. Such candidates don't meet criteria for the highest priority status, and tend to get much sicker while on the waiting list than other candidates.

Discussion Summary

The Committee Vice Chair discussed the need to address a select group of pediatric candidates as part of the Committee's continuous distribution work. The group in question are pediatric candidates who are greater in size than neo-natal patients, and smaller in size than small adults. They are experiencing similar issues as adult status 2, 3, and 4 candidates in that the inadequate supply of donor hearts is preventing them from getting donor hearts, despite have fairly high medical urgency. This group of pediatric patients won't be able to access donor hearts because other candidates with greater medical urgency will keep moving ahead of them.

The Vice Chair said that the Committee might need to consider a way to combine waiting time and medical urgency to give this group of pediatric candidates additional priority, like the Committee is considering for waiting time on LVAD. The Chair said the Committee might also want to consider addressing the group through medical urgency alone. Another option could be to try and address the issue through a waiting time attribute that would apply to both pediatric and adult candidates. Waiting time could also be used break ties when equal composite allocation scores were calculated. The Vice

Chair suggested that additional priority for the group of pediatric candidates in question might also be addressed through the use of patient access.

Next Steps

Committee members will be asked to identify ways to give greater priority in the continuous distribution allocation framework for this group of pediatric candidates.

4. Reminder of 09/22 in-person meeting and closing remarks

Discussion Summary

The Committee members were reminded that the in-person meeting is scheduled for 09/22/2023 in Detroit, Michigan, and that the Committee will meet for dinner on 09/21/2023.

Upcoming Meeting(s)

- September 6, 2023 (teleconference)
- September 22, 2023 (in-person)
- October 4, 2023

Attendance

- **Committee Members**
  - Rocky Daly, Chair
  - J.D. Menteer, Vice Chair
  - Amrut Ambardekar
  - Jennifer Carapellucci
  - Jennifer Cowger
  - Tim Gong
  - Eman Hamad
  - Jennifer Hartman
  - Cindy Martin
  - Nader Moazami
  - Martha Tankersley
  - Dmitry Yaranov
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Daniel Thompson
- **SRTR Staff**
  - Yoon Son Ahn
  - Monica Colvin
  - Ryo Hirose
  - Grace Lyden
  - Katie Siegert
- **UNOS Staff**
  - Alex Carmack
  - Cole Fox
  - Elena Liberatore
  - Kelsi Lindblad
  - Alina Martinez
  - Eric Messick
  - Holly Sobczak
- **Other Attendees**
  - Andrew Flescher, OPTN Ethics Committee Chair
  - Shelley Hall
  - Ted Papalexopoulos
  - Stephanie Taylor
  - Daniel Yip