OPTN Liver and Intestinal Organ Transplantation Committee
Meeting Summary
September 30, 2022
Conference Call

James Pomposelli, MD, PhD, Chair
Scott Biggins, MD, Vice Chair

Introduction

The OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 09/30/2022 to discuss the following agenda items:

1. Continuous Distribution Attribute Re-cap: Hepatocellular Carcinoma (HCC) Stratification
2. Continuous Distribution Attribute Re-cap: Willingness to Accept a Split Liver
3. Continuous Distribution Attribute: Donor-Recipient Size Matching

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

1. Continuous Distribution Attribute Re-cap: Hepatocellular Carcinoma (HCC) Stratification

The Committee reviewed their discussions from the September 16, 2022 Committee meeting, and continued discussing hepatocellular carcinoma (HCC) stratification as a potential attribute to incorporate into continuous distribution of livers and intestines.

Summary of discussion:

Summary of September 16, 2022 discussions:

- Currently, all transplant candidates qualifying for standardized HCC exception receive median MELD at transplant (MMaT) minus three
- Currently, HCC encompasses about thirteen to twenty percent of the liver waitlist and transplant
- There are various models to stratify waitlist dropout risk for HCC transplant candidates
- Stratifying HCC transplant candidates based on urgency/benefit rather than one common score addresses final rule regulations
    - Prioritizing transplant candidates by urgency, optimizes utility of transplant, and preserves access for transplant candidates with HCC
- At a certain threshold, higher waitlist risk associated with increased post-transplant mortality and HCC recurrence
- May need to consider post-transplant outcome (utility) and overall transplant benefit
    - Current system sets a ceiling of alpha fetoprotein (AFP) greater than 1,000, outside Milan criteria, and extrahepatic disease
- Matching HCC waitlist dropout risk to non-HCC may decrease access to transplant further for HCC transplant candidates
    - HCC waitlist dropout risk matched to MELD score is generally lower (most MELD-HCC less than 20)
- HCC is not only about waitlist dropout but also about access and window for transplant
- A model for HCC stratification should include MELD, tumor size/burden, AFP, wait time

    - If time served is not included, then may disincentives locoregional treatment to control tumor
- Simple stratification may be preferable to more complex algorithms
    - Added complexity may not be necessary to appropriately risk stratify
    - Categories versus continuous scoring
    - Adding in dynamic variables, such as tumor growth, may disincentive treatment

The Chair stated that HCC transplant candidates should be stratified in the points-based allocation system. The Chair asked about the ability to interdigitate HCC transplant candidates with MELD transplant candidates. The Chair stated that Optimized Prediction of Mortality (OPOM) may allow for this ability and noted that the Committee will receive a presentation on the function of OPOM at the next Committee meeting.

Next steps:

The Committee will continue to discuss HCC stratification as a potential attribute in the continuous distribution of livers and intestines.

2. Continuous Distribution Attribute Re-Cap: Willingness to Accept a Split Liver

The Committee reviewed their discussions from the September 9, 2022 Committee meeting, and continued discussing willingness to accept a split liver as a potential attribute to incorporate into continuous distribution of livers and intestines.

Summary of discussion:

Summary of September 9, 2022 discussions:

- Split liver transplantation is a critical means of access for transplant for small children
    - Split liver transplantation survival equivalent to living donor liver transplantation
    - Split liver transplantation confers survival advantage for pediatric transplant candidates less than seven kilograms
- Split liver transplantation is underutilized relative to its potential impact on children and adults
    - Historically around three percent of transplant
    - Declined to around two percent after implementation of acuity circles (AC)
    - Split liver transplantation is performed at about twenty transplant programs
- Policy initiatives and variances have not increased split liver transplantation utilization
    - Current allocation policy complicates split liver transplantation utilization, especially related to place of the second segment
- Significant transplant program concerns remain regard split liver transplantation complexity and risk
    - Split liver transplant for adults restricted in practice to lower model for end stage liver disease (MELD) score transplant candidates
    - Adult transplant candidates rarely initiate split liver transplantation
- Deceased donors that meet “splittable” criteria should trigger a primary match run with allocation points given to pediatric and short stature candidates who will accept a split liver transplantation
    - Current “splittable” criteria: age less than forty, single vasopressor or less, transaminases equal to or less than three times normal, body mass index (BMI) equal to or less than twenty eight

    - Majority of split liver donors are age less than thirty, BMI equal to or less than 25[1]
- Allow expedited placement of second segment on a separate match run, to transplant programs and transplant candidates who will accept a split
- Give "proximity" points to the primary transplant program (or associated adult transplant program of a pediatric transplant program) in the match run for the second segment
- Consider additional points for transplant candidates at a transplant program with history of split liver transplantation utilization

The Chair asked for the rationale behind creating a separate match run for split liver allocation. A member responded that a catered match run for the second segment may help expedite allocation. The member explained that current practice requires organ procurement organizations (OPOs) to use the same match run to allocate the second segment which causes logistical issues that may impend the utilization of the second segment. The member recognized that modification to policy language may address these previously mentioned logistical issues, but the member stated that creation of a new match run is a novel idea that may address it as well.

Another member suggested that incentivizing transplant programs as well as small statured adults in a mutually beneficial way may increase split liver utilization. The member explained that transplant candidates could be incentivized by providing higher MELD scores for the risk and transplant program could be incentivized by being allowed to keep the liver at their own program. The Chair noted that *Policy 9.12.C: Closed Variance for Any Segment Liver Transplantation* was intended to address that. The Chair recognized that split liver transplants have decreased since the implementation of AC.

A member of the community suggested that the smallest pediatric transplant candidates should be prioritized. The member explained that data shows the highest waitlist mortality in pediatric population is in the children zero to two years of age. The Chair of the OPTN Pediatric Committee agreed and noted support.

Next steps:

The Committee will continue to discuss willingness to accept a split liver as a potential attribute in the continuous distribution of livers and intestines.

3. Continuous Distribution Attribute: Donor-Recipient Size Matching

The Committee discussed donor-recipient size matching as a potential attribute to incorporate into continuous distribution of livers and intestines.

Summary of discussion:

Research and input compiled from Committee members prior to this meeting included:

- Donor-recipient size matching as a potential attribute in continuous distribution intends to address inherent biological disadvantages (i.e. size) that particularly affect small transplant candidates on the waitlist
- There are many ways to measure size
    - Height and body surface area are currently collected

[1] Perito ER at al. Transplantation 2019;103:5520557

    - Anteroposterior (AP) diameter is not currently collected for either deceased donors or transplant candidates
    - Female sex is noted as not a measure of size but often used as a surrogate in studies
- Deceased donor and transplant candidate height distributions are the same
- Smaller transplant candidates have lower transplant rates and higher mortality[2]
- Transplant candidates who are five feet or shorter have about a forty-two percent transplant rate while those who are five foot and seven inches or taller have about a fifty-four percent transplant rate[3]
    - Inverse relationships for waitlist dropouts for death or too sick with higher rates for the shortest transplant candidates and lower rates for the tallest transplant candidates
- A study focused on waitlist outcomes by body surface area observed that the smallest body surface area (BSA) group had about a forty-six percent transplant rate while the largest BSA group had about a fifty-seven percent transplant rate[4]
    - This study observed a similar inverse relationship for waitlist dropouts for death or too sick as the study above observed
    - The study model showed that the smallest twenty five percent of transplant candidates appear to be disadvantaged
- MELD predicts death on the waitlist; Size is about access to deceased donors
- In multivariable models, women were more likely to have an organ offer declined while in the first position, second position, or third position[5]
    - This difference disappeared when BSA, height, estimated liver weight(eLW), or estimated liver volume (eLV) were added to the model
- Overall acceptance rates for adult deceased donor livers offered first to women was forty-eight percent and those offered first to men was eighty percent[6]
- Adjusting for BSA, eLV, or eLW decreased the disparity between men and women by forty to fifty percent
    - Anthropometric (AP) measurements more strongly associated with deceased donor liver transplant inequities than MELD and geography[7]
- Split liver transplant may help some, if small transplant candidates receive priority
    - Split liver transplantation would only benefit transplant candidates at transplant programs willing to accept split livers

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[2] Bernards S, Lee E, Leung N, Akan M, Gan K, Zhao H, Sarkar M, Tayur S, Mehta N. Awarding additional MELD points to the shortest waitlist candidates improves sex disparity in access to liver transplant in the United States. Am J Transplant. 2022 Jul 24. doi: 10.1111/ajt.17159.

[3] Ibid.

[4] Kling, et al. (JAMA Surg, under revision).

[5] Nephew LD, Goldberg DS, Lewis JD, Abt P, Bryan M, Forde KA. Exception Points and Body Size Contribute to Gender Disparity in Liver Transplantation. Clin Gastroenterol Hepatol. 2017 Aug;15(8):1286-1293.e2. doi: 10.1016/j.cgh.2017.02.033.

[6] Ge J, Gilroy R, Lai JC. Receipt of a pediatric liver offer as the first offer reduces waitlist mortality for adult women. Hepatology. 2018 Sep;68(3):1101-1110. doi: 10.1002/hep.29906.

[7] Locke JE, Shelton BA, Olthoff KM, Pomfret EA, Forde KA, Sawinski D, Gray M, Ascher NL. Quantifying Sex-Based Disparities in Liver Allocation. JAMA Surg. 2020 Jul 1;155(7):e201129. doi: 10.1001/jamasurg.2020.1129.

    - Modeling shows that if all split livers qualify as "Splittable" were actually split, the disparity would be overcome.[8] However, was noted this is not feasible due to many practical and logistical reason.
- Donor-recipient size matching as an attribute would impact various sizes of populations depending on how "small" is defined
    - Small defined as less than 166 centimeters would impact about thirty-six percent of the population[9]
    - Small defined as less than 157 centimeters would impact about seven point eight percent of the population[10]
    - One study's proposed solution would benefit the smallest fifteen percent of the population[11]
- Donor-recipient size matching as an attribute in continuous distribution would impact disadvantaged groups
    - Female transplant candidates
    - Hispanic and Asian transplant candidates
- A study analyzed height less than 166 centimeter as a cut off for priority points using competing risk regression of difference in waitlist mortality by height[12]
- Another study analyzed giving additional MELD points by height group[13]
- A study modeled prioritizing low BSA deceased donors to low BSA transplant candidates[14]
- Another study analyzed multivariable competing risks analysis of waitlist mortality and observed that females had a higher risk of waitlist mortality when receiving an adult first offer, but not for pediatric first offer[15]
- The OPTN currently collects height and weight, but not data related to deceased donor and transplant candidate AP diameter

The Chair stated that adding additional MELD points to address size disparities may not be the correct solution. The Chair explained that the points-based system will address various attributes, in addition to MELD, therefore adding additional points to MELD may be diluted.

A member of the community stated that to overcome the size disparity, small deceased donors need to be carved out. The member of the community noted that increasing split liver utilization and prioritizing pediatric transplant candidates will help address the disparity, but it will not resolve it.

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[8] Kling et al. JAMA Surg (in revision)
[9] Ge J, Lai JC. Identifying a clinically relevant cutoff for height that is associated with a higher risk of waitlist mortality in liver transplant candidates. Am J Transplant. 2020 Mar;20(3):852-854. doi: 10.1111/ajt.15644.
[10] Bernards S, Lee E, Leung N, Akan M, Gan K, Zhao H, Sarkar M, Tayur S, Mehta N. Awarding additional MELD points to the shortest waitlist candidates improves sex disparity in access to liver transplant in the United States. Am J Transplant. 2022 Jul 24. doi: 10.1111/ajt.17159.
[11] Kling, et al. (JAMA Surg, under revision).
[12] Ge J, Lai JC. Identifying a clinically relevant cutoff for height that is associated with a higher risk of waitlist mortality in liver transplant candidates. Am J Transplant. 2020 Mar;20(3):852-854. doi: 10.1111/ajt.15644.
[13] Bernards S, Lee E, Leung N, Akan M, Gan K, Zhao H, Sarkar M, Tayur S, Mehta N. Awarding additional MELD points to the shortest waitlist candidates improves sex disparity in access to liver transplant in the United States. Am J Transplant. 2022 Jul 24. doi: 10.1111/ajt.17159.
[14] Kling, et al. (JAMA Surg, under revision).
[15] Ge J, Gilroy R, Lai JC. Receipt of a pediatric liver offer as the first offer reduces waitlist mortality for adult women. Hepatology. 2018 Sep;68(3):1101-1110. doi: 10.1002/hep.29906.

A member noted that the implementation of MELD 3.0 will incorporate a sex variable to address some of the size disparity. The member stated that incorporating additional size-related attributes will need to be considered in the context of integrating with what MELD 3.0 is intending to address. The member of the community responded that MELD 3.0 intends to address waitlist mortality while incorporating size as an attribute in the context of continuous distribution intends to address access to liver transplant.

A member suggested incorporating prioritization for size by identifying a range of MELD scores that increases priority for donor-recipient size matching. The Chair agreed and suggested the Committee could consider that size prioritization occurs as waitlist mortality increases.

Next steps:

The Committee will continue to discuss willingness to accept a split liver as a potential attribute in the continuous distribution of livers and intestines.

Upcoming Meeting

- October 7, 2022 @ 3:00 PM ET (teleconference)
- October 11, 2022 @ 9:00 AM CT (Chicago, IL)

Attendance

- **Committee Members**
  - Alan Gunderson
  - Allison Kwong
  - Christopher Sonnenday
  - Colleen Reed
  - Erin Maynard
  - Greg McKenna
  - James Markmann
  - James Perkins
  - James Pomposelli
  - James Trotter
  - Joseph DiNorcia
  - Kym Watt
  - Neil Shah
  - Peter Abt
  - Shunji Nagai
  - Sophoclis Alexopoulos
  - Vanessa Pucciarelli
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - John Lake
  - Katie Audette
  - Nick Wood
  - Ryo Hirose
- **UNOS Staff**
  - Julia Foutz
  - Krissy Laurie
  - Matt Cafarella
  - Megan Oley
  - Meghan McDermott
  - Niyati Upadhyay
  - Sarah Scott
  - Susan Tlusty
- **Other Attendees**
  - Catherine Kling
  - Dave Weimer
  - Emily Perito
  - Pratima Sharma
  - S DeLair
  - Samantha Taylor