

Liver and Intestinal Organ Transplantation Committee
July 21, 2011
Interim Report

1. Committee Orientation: The Committee received a brief orientation to the OPTN structure and Committee and Board processes. This included a review of the responsibilities of the regional representatives as the chairs of their Regional Review Boards (RRBs). Committee members expressed a need to educate the RRB chairs and RRB members regarding submission and review of standardized MELD/PELD exception cases.
2. Approved Committee Projects: During their June 2011 meeting, the Executive Committee approved eight projects (new and ongoing) that the Committee will be working on in 2011-2012:
 - Further development of policies to reduce geographic disparities in waiting list mortality
 - Ongoing review of MELD/PELD exceptions
 - Additional priority for DCD recipients that require retransplant
 - Facilitated placement / reduced discards
 - Enhancements to the MELD score / Liver allocation
 - Ongoing review of Status 1A/B cases not meeting criteria
 - Allocation of livers for hepatocyte transplants
 - Intestinal surgeon/physician criteria
3. Subcommittees. The Committee has the following Subcommittees and Working Groups:
 - MELD Enhancements Subcommittee
 - Liver Utilization Working Group
 - HCC Subcommittee
 - Status 1 Review Subcommittee
 - Intestine Issues Working Group
 - Joint Pediatric-Liver Committee Subcommittee
 - Distribution Subcommittee

Open subcommittee positions will be populated with new committee members.

4. Review of Comments Received on Proposals Circulated for Public Comment: The Committee reviewed comments received on three proposals the Committee circulated for public comment in March 2011.

Proposal for Improved Imaging Criteria for HCC Exceptions: Of the 32 individual comments received, 69% with an opinion (n=26) were in support of the proposal. All regions except Region 4 were in support of the proposal. Only the Patient Affairs Committee voted on the proposal, with a vote of support. ASTS and NATCO indicated their support.

Comments in opposition to the proposal were mostly related to additional costs and data burden. However, the proposal should not increase costs or data burden, except for the requirement for outside scans to be repeated at the transplant center. No additional data submission is required, and an optional template is provided for ease of documentation. Further, a survey of all programs in 2010 indicated that more than 70% of images are already being read or performed at the transplant center, and 90% of respondents indicated that the requirements in the proposal were similar to what they are currently doing. There were some concerns about how UNOS would monitor the minimum technical standards in Table 4 and 5; however, these were recommended as guidelines, not requirements. The proposal will be amended to clarify that Tables 4 and 5 are recommended, but not required.

The American College of Radiology's LI-RADS (Liver Imaging - Reporting and Data System) Committee, which has developed a similar but not identical classification system for HCC imaging, sent a letter opposing the proposal as written. The LI-RADS criteria are tailored for diagnosis of HCC, while the proposed OPTN policy criteria are tailored for identifying candidates with HCC that are eligible for automatic exception points for liver transplantation. The current proposal described OPTN Class 0-5, but only Classes 0 (incomplete or technically inadequate study) and 5 (meets radiologic criteria for HCC) are relevant to the policy, while 1-4 are diagnostic. The subtle differences between the OPTN proposal and the LI-RADS recommendations were resolved via a conference call on July 20, 2011. As a compromise, the policy will be modified to reflect only OPTN classes 0 and 5, and Table 6 will be simplified to remove differences between the two systems, with reference to LI-RADS.

The Committee agreed to forward the proposal as amended to the Board by a vote of 21 in favor, 1 opposed, and 3 abstentions. The Committee members suggested that the LI-RADS group be asked to better tailor their Class 5 to the OPTN Class 5 going forward.

Proposal to Reduce Waiting List Deaths for Adult Liver-Intestine Candidates: Of the 25 individual comments received, 83% with an opinion (n=18) were in support of the proposal. Regions 1,4,5,6, and 11 were in support of the proposal, and Region 2 supported it with amendment. Regions 3, 7, 8,9,10 did not support the proposal. The Organ Availability and Pediatric Committees supported the proposal while the Patient Affairs Committee did not. ASTS and NATCO indicated their support. Comments in opposition to the proposal included (Committee responses in italics):

- Why not award more points to adults? *This is already in place; adults receive a score equivalent to a 10% increase in their mortality risk.*
- There should be a floor for the MELD score assigned to the patients. *Currently with the 10% increase, the lowest MELD score that is assigned is 20.*
- Will adversely impact small-statured adult. *This was addressed in proposal; these candidates have an elevated risk of waiting list mortality, but not nearly as high as those waiting for a Liver-Intestine.*
- What about the poor post-transplant outcomes? *Data presented at ATC showed that there is a net benefit to transplanting these patients due to their high waiting list mortality.*

The Committee agreed to forward the proposal to the Board in November by a vote of 21 in favor, 1 opposed, and 1 abstention. The Committee will review the impact of the proposal two years after implementation, especially the affect on small statured adults.

Split Liver CAS: Of the 24 individual comments received, 100% with an opinion (n=17) were in support of the proposal. All regions were in support of the proposal. The OPO, Patient Affairs, and Transplant Coordinators Committees supported the proposal. The Pediatric Transplantation Committee did not support the proposal, for the same reasons the Committee did not support the Region 2 and OneLegacy AAS' upon which this was modeled. ASTS and NATCO indicated their support. The Committee will follow up with the Pediatric Committee to determine if there is a misunderstanding of the proposal or issues that can be resolved. The Committee voted to forward the proposal to the Board by a vote of 23 in favor, 0 opposed, and 1 abstention. A plan will be developed to advertise this and to enroll participants if approved.

5. Ongoing Policy Development for Broader Distribution of Livers: The SRTR provided a brief tutorial about the LSAM model and a review of LSAM modeling data for share 15 National and tiered Regional Sharing. The Committee also received a review of the Sharing Threshold (ST) concept. The Committee had asked the SRTR to model the impact of a "Share 15 national" policy, as well as

regional sharing for MELD/PELD scores for 35 or greater. The SRTR was also asked to model a regional share for MELD/PELD scores of 32 and higher. Both regional proposals were modeled with sharing thresholds of 0, 1, 2, and 3, and in combination with the Share 15 National policy.

The Committee reviewed the results of 18 separate models, including the current policy. For each scenario, the SRTR provided the number of total deaths and waiting list deaths, the percent of organs shared outside the local unit, and the median distance organs traveled. The greatest decrease in total deaths was seen with Share 15 National combined with the Regional Share 32. The reduction in waiting list deaths was significant ($p=0.001$). The change in total deaths was not statistically significant. Most of the benefit was derived from the Share 15 National, with most of the decreases in total deaths due to decreases in waiting list deaths. The impact of the various sharing thresholds (0,1,2,3) is indeterminate, as the number affected by the threshold is small. There were minimal increases in the median distance an organ traveled across the proposals modeled. The Committee asked the SRTR to provide the median distance traveled for organs that shared outside the local area, rather than for all transplants.

The Committee reviewed a letter from Kathleen Sebelius, Secretary of the U.S. Department of Health and Human Services, requesting that “the OPTN develop one or more variances to demonstrate the efficacy of broader distribution of livers with the goal of reducing intertransplant program variation on appropriate clinical endpoints such as mortality on the waitlist and MELD at time of transplant.” Any variance must be in accordance with the Final Rule and OPTN policies. Further, any variance approved by the OPTN must “be designed in a scientific manner with the goal of demonstrating the impact of broader distribution policy options on clear end-points (e.g., reduced mortality of candidates on the waiting list.” The Committee reviewed the evidence gathered to support the Share 15 National and Share 35 regional proposals. In addition to the LSAM modeling, the Committee cited analyses indicating that candidates with MELD scores of 35-40 have mortality rates similar to those in Status 1, and Regional Status 1 distribution has been in place since December 2010. Further, there has been a large reduction in waiting list deaths since Share 15 Regional was implemented in August 2005. The Committee feels that Share 15 has been well-demonstrated in all 11 regions since that time.

HRSA representatives in attendance described this as a request from the Secretary for the OPTN to take a more proactive approach within the context of the requirements of the OPTN Final Rule and the directive and guidance HHS received from Congress in the 2010 conference report. The report lists a number of requirements that must be met before the OPTN can enact any changes to the liver distribution policy. One of the key requirements is that it must be designed to show reasonable efficacy that can be demonstrated before enacted nationally. The letter further articulates the constraints that the OPTN is under by direction of Congress. The letter does not stipulate statistical significance, because sometimes that is not possible to achieve. It was further noted that the language was limited to broader distribution, and so would not apply to a change in the MELD score, for example. The Committee could revise the definition of Status 1 to include Candidates listed with a MELD score of 35 and above, based on the mortality data cited. This would be a change to allocation and not distribution and thus not subject to the requirements of the report language.

The Committee discussed each proposal separately. Based on the evidence described earlier, the Committee approved a motion to circulate the Share 15 National proposal for public comment by a vote of 23 in favor, 0 opposed, and 1 abstention.

The Committee discussed whether the proposal for a Regional Share 35 with a sharing threshold of 3 should move forward. A motion to do so was made and seconded. Committee members discussed the need for a sharing threshold, which adds complexity, but would have a very small impact based

on the modeling results. The sharing threshold may make people comfortable that livers will not be crossing in the air for similarly ill patients, which also adds to cost.

The Committee discussed the notion of a change definition of Status 1. This would accomplish the same goal with the same patient population. The Committee reviewed the death rates for these candidates, which are significantly higher than candidates with lower scores. Committee members were concerned that altering the definition of Status 1 would not be supported by the community. The current Status 1 definition typically includes patients who have sudden onset of disease and do well with a transplant, while the patients with MELD scores of 35 or higher, while equally sick, are usually chronically ill patients who do not do as well. Thus, while the mortality risk is similar, the candidates are not similar in terms of outcomes. However, Committee members also felt they should heed the advice they had been given. The category could be called “Status 1 MELD” and possibly include a sharing threshold. The motion for Regional Share 35 was withdrawn after discussion.

A new motion was made to create a Status 1 MELD category for those candidates with calculated MELD scores of 35 and higher. This category would fall after the Status 1As and 1Bs. The model that most closely represents this concept is the Share 35 with a ST of 0. Under this model, organs are offered by MELD score, with local always before regional at each score. The Committee agreed with the sequence as modeled. This motion was approved by a vote of 22 in favor, 1 opposed, and 1 abstention.

The Committee discussed whether Status 1MELD should include exceptions. The motion approved would apply to calculated MELD scores only, while the modeling data reviewed included exceptions. Some of the exceptions in this category are those with HAT that receive a MELD exception score of 40. It was noted that most candidates with exceptions are transplanted before reaching a MELD score of 35, and that those cases could be reviewed by the Status 1 Review Subcommittee. A new motion to consider including all candidates with MELD/PELD scores of 35 or higher was made and seconded. This motion was approved by a vote of 22 in favor, 2 opposed, and 1 abstention. The public comment proposal will ask specifically whether exceptions should be included.

The Committee asked the SRTR to provide the following additional analyses:

- The median distance traveled by organs that were shared overall and at MELD/PELD 35 and above with and without the Share 15 national system
- The percentage of organs shared overall and at MELD/PELD 35 and above with and without the Share 15 national system.
- The number of lives saved per organs shared compared to the current system.
- Waitlist mortality for MELD/PELD 35+ candidates compared to Status 1A and 1B candidates
- Post transplant survival outcomes (graft and patient) of patients with MELD 35-40 compared to Status 1A, 1B

When possible, the Committee asked for LSAM data by region as well as overall, and for time periods of time beyond one year. The Committee also requested the following: the number of candidates ever waiting during a year with MELD/PELD scores 35 and higher, the number of patients transplanted at the scores, and the number waiting on a snapshot with these scores. All analyses should also be stratified by diagnosis, MELD/PELD exception (yes/no) and adult versus pediatric.

Subcommittee/Working Group Updates

6. Liver Utilization Working Group: The Committee received a brief update on the efforts of the Liver Utilization Working Group. This Working Group has been reviewing data in order to identify factors

related to expedited placement. The Working Group has also identified a subset of expedited placements that occurred between specific OPO/center combinations. The Group has been working with the Effective Screening Work Group to identify centers that routinely turn down offers for certain types of donors, despite acceptance criteria indicating the center would accept such offers. This analysis was already performed for kidney transplant programs; letters were sent to kidney programs to encourage centers to use realistic acceptance criteria.

7. Status 1 Review Subcommittee: The Committee reviewed the process that has been in place since August 2010. Status 1A and 1B cases that do not meet criteria are reviewed by the Status 1 Subcommittee soon after listing. Reviews and votes are conducted using the UNetSM Committee Management System. If a listing is found to be inappropriate by a majority vote, the center is given the option to downgrade the patient, appeal the decision and provide more information, or keep the candidate at the status (with referral to the Liver Committee and possibly the Membership and Professional Standards Committee). In some instances, centers choose to ask the Subcommittee to vote prior to listing the patient. Between November 2010 and May 2011, 27 candidates were listed who did not meet criteria. Of those, only 1 was transplanted in that status.
8. Re-execution of the Match System Subcommittee: In 2010, The Department of Evaluation and Quality (DEQ) asked the Committee to better define when re-execution of the liver match is appropriate. The current policy allows for re-execution if there is a „change in specific medical information related to the liver donor,‘ which is not well-defined. The Subcommittee is revising the policy language, as much of it is outdated. The Subcommittee has asked for the reasons the match has been re-executed in the past, to make sure that it considers all reasonable situations. If this is not possible, the Subcommittee requests that DEQ keep a list of the reasons moving forward.
9. MELD Enhancements and Exceptions Subcommittee: Earlier in the year, the Subcommittee asked that the SRTR update the MELD-Na analysis published in the New England Journal of Medicine (NEJM). The revised results were similar to those published in the NEJM, with updated lower and upper bounds for sodium of 125 and 137 mmol/L. There is an 8% increased risk of death per unit decrease in serum sodium concentration between 137 and 125 mmol/L (RR = 1.08, 95% CI 1.07-1.09, p<0.001). The effect of serum sodium is greater in candidates with lower MELD scores. The SRTR is currently working on requests to refit the current MELD equation, the MELD-Na equation, and to assess the impacts of each using both.
10. Member Request Regarding Allocation of Hepatocytes: The Committee will work with the OPO Committee to further address this issue, as there may be an opportunity to educate the OPOs about the current policy. Centers with these listings will also be contacted to ensure that they are being listed appropriately.

**Committee Participation
July 21, 2011**

Kim Olthoff, MD	Chair	X
David C. Mulligan, MD	Vice Chair	X
Shimul A. Shah, MD	Regional Rep. Region 1	X
Andrew Cameron, MD	Regional Rep. Region 2	X
Brendan McGuire, MD	Regional Rep. Region 3	X
Mark R. Ghobrial, MD, PhD	Regional Rep. Region 4	X
Johnny C. Hong, MD	Regional Rep. Region 5	X
Jorge D. Reyes, MD	Regional Rep. Region 6	By phone
David C. Cronin, II, MD, PhD	Regional Rep. Region 7	X
Michael D. Voigt, MB, ChB	Regional Rep. Region 8	X
Lewis Teperman, MD	Regional Rep. Region 9	By phone
John Fung, MD, PhD	Regional Rep. Region 10	X
Michael Marvin, MD	Regional Rep. Region 11	X
Tom Mone	At Large	X
Kim Brown, MD	At Large	X
Kareen Abu-Elmagd, MD	At Large	X
Michael Charleton, MD	At Large	By phone
James Trotter, MD	At Large	X
James Eason, MD	At Large	X
Simon P. Horslen, MB, ChB	At Large	
Goran B. Klintmalm, MD, PhD	At Large	X
Thomas Starr	At Large	X
Fredric G. Regenstein, MD	At Large	X
Srinath Chinnakotla, MD	At Large	X
Ryutaro Hirose, MD	At Large	By phone
Julie Heimbach MD	At Large	X
James Bowman, MD	Ex Officio, HRSA	X
Richard Durbin	Ex Officio, HRSA	By phone
Monica Lin, PhD	Ex Officio, HRSA	By phone
Ba Lin, PhD	Ex Officio, HRSA	By Phone
Peter Stock, MD	MMRF, SRTR Representative	X
Yi Peng, MS	MMRF, SRTR Representative	X
Jon Snyder, MD	MMRF, SRTR Representative	By phone
W. Ray Kim, MD	MMRF, SRTR Representative	By phone
Bertram Kasisky, MD	MMRF, SRTR Representative	By phone
Maureen McBride, PhD	UNOS, Director of Research	By phone
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
Ann Harper	UNOS, Policy Analyst	X
Lee Goodman	UNOS IT Department	X