

**OPTN Liver and Intestinal Organ Transplantation Committee
National Liver Review Board (NLRB) Subcommittee**

July 25, 2024

Conference Call

James Pomposelli, MD, PhD, Chair

Introduction

The OPTN National Liver Review Board Subcommittee (the Subcommittee) met via WebEx teleconference on 07/25/2024 to discuss the following agenda items:

1. Update on New Project: Update NLRB Guidance + Further Alignment with Liver Imaging Reporting and Data System (LI-RADS)

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

1. Update on New Project: Update NLRB Guidance + Further Alignment with Liver Imaging Reporting and Data System (LI-RADS)

The Subcommittee discussed their new project focused on updating the Adult Model for End-Stage Liver Disease (MELD) Exception Review guidance document and updating hepatocellular carcinoma (HCC) policy and guidance to align with LI-RADS 5 terminology as well as the addition of contrast-enhanced ultrasound.

Summary of discussion:

Contrast-Enhanced Ultrasound (CEUS) & LI-RADS Alignment

The Subcommittee discussed follow-up questions regarding the addition of CEUS and alignment of LI-RADS 5 into HCC policy and guidance.

The Subcommittee discussed the starting point for the previously identified 90 calendar day timeframe for when a CEUS should be performed in relation to a CT or MRI. A member suggested that 90 days before or after a CT or MRI could be acceptable. The member added that the CT or MRI could occur on the same date as the CEUS and that would also be acceptable. Another member asked whether a CEUS needs to be performed in instances when additional CTs or MRIs are performed that occur outside of the 90 day timeframe. A member responded that the CEUS is an adjunct diagnostic tool, and it does not seem that it would be necessary to repeat a CEUS. Another member added that the use of CEUS can be compared to that of a biopsy. The member explained that if there is an LR-M and it is biopsied to diagnosis HCC, it would not be biopsied again in the future. The member stated the CEUS provides an additional piece of information that helps make a diagnosis and the subsequent CT or MRI scans are mostly to document progression or new lesions. Another member agreed that the CEUS should not need to be repeated and emphasized that the policy language makes that clear. A member stated that the timeframe of the CEUS should be tied to the CT or MRI that is being used to help make a diagnosis for initial exception requests but does not need to be repeated for extensions.

The Subcommittee discussed whether these modifications apply to the pediatric population as well and a member suggested that colleagues from the OPTN Pediatric Transplantation Committee and American College of Radiology be asked for guidance.

The Subcommittee discussed the possibility of CT and MRI having results that are outside of criteria in policy while the CEUS aligns with criteria in policy. A member stated that the CEUS is an adjunctive diagnostic tool and would not be reliable to provide information related to size or number of lesions, which is provided through CT or MRI. A member agreed and stated that the CT or MRI should be used to provide information related to size of the lesions, not the CEUS. Another member stated that the policy could state that Milan criteria are based on cross-sectional imaging to ensure it is clear that CT or MRI needs to provide this information. A member suggested the policy could state that for the purposes of size, cross-sectional imaging would be the preferred modality used to assess size and Milan criteria.

The Subcommittee discussed utilizing the terminology of dynamic or multiphase. A member stated that the colleagues from American College of Radiology suggested to use multiphase. Members agreed that the policy should modify the use of dynamic to multiphase.

The Subcommittee discussed whether policy should clarify type of CEUS such as b-mode CEUS. A member stated that it does not appear necessary to specify b-mode CEUS in policy.

The Subcommittee reviewed the HCC exception form and discussed how to accurately capture the modifications related to LI-RADS 5 to ensure that policy and the system are in alignment. A member suggested that the collection be termed "LI-RADS 5 on CT or MRI with or without CEUS". Another member suggested that the collection could be two separate indications, one stating "LI-RADS 5 on CT or MRI" and the other stating "LI-RADS 5 in combination of CT or MRI with CEUS".

Updating NLRB Guidance

The Subcommittee reviewed diagnoses in the Adult MELD Exception Review guidance document and discussed potential modifications.

Hepatic Epithelioid Hemangioendothelioma (HEHE)

A member noted that the most pertinent points in the current NLRB guidance for HEHE include that it is unresectable and that guidance does suggest a biopsy. The member stated that while it does clarify that extrahepatic disease is not necessarily a contraindication, that is based on a small report from the ELTR from about 17 years ago that included ten patients with extrahepatic disease. However, the member noted that the number of patients with extrahepatic disease is not well documented in the literature.

The member reviewed recent literature and noted there are some emerging systemic therapies which may change the landscape for non-standard exceptions for candidates with HEHE. The member noted another article that was a small single-center study that observed a 64% overall five year survival if there was no extrahepatic disease. The member reviewed another article that observed that the disease free and overall survival statistics are better than most of the other neoplasms that are indications for transplant. The member noted that this study found that microvascular invasion was not an adverse prognostic risk factor for recurrence but macrovascular invasion was a strong risk factors. The member stated that literature also found that a shorter waiting period was associated with a higher recurrence rate. The member stated that literature also noted that hilar lymph node involvement increased the risk of occurrence about two fold.

Based on the review of recent literature, a member suggested that the statement regarding the impact of microvascular invasion should be removed from guidance as it is no longer accurate. The member suggested a score recommendation of MMaT minus three due to the small numbers of transplants.

Another member stated that the Subcommittee should be recommending guidance that describes criteria for accessing MELD exceptions and not creating guidance that proscribes therapy or treatment of clinical conditions. A member agreed it may be too early to describe criteria related to progression or therapy since it is still being studied in the literature. Another member agreed that the guidance should not be too prescriptive as transplant programs are likely monitoring these candidates very closely to ensure transplant is the right option at the right time.

Another member stated that the literature does make a compelling case for including macrovascular invasion as a contraindication. A member noted that including this in guidance would mean that the candidates should not receive the exception points, but they could still receive a transplant. Another member suggested that the guidance could note that candidates with macrovascular invasion have a higher risk, but still let the transplant program decide whether they choose to submit an exception in those cases. The member stated that if macrovascular invasion is indicated as a contraindication for transplant in the guidance document, there needs to be strong data to support it. A member responded that the literature highlights an association, but it is a small number of patients.

Another member stated that the recurrence of HEHE is that which recurs over years and should not impact early post-transplant outcomes. Members agreed that a statement regarding macrovascular invasion should be cautionary to allow transplant program and NLRB reviewer discretion when submitting and reviewing cases.

A member stated that the NLRB guidance should not serve as educational pieces but to outline clear criteria for non-standard exceptions. The member asked if the HEHE guidance requires any modifications to help streamline the language. Another member responded that they will modify the guidance for clarity and bring back to the Subcommittee for further review.

Budd Chiari

A member who reviewed the Budd Chiari section stated that the current guidance reads well and no changes are necessary beyond adding a score recommendation. The member suggested MMaT minus three as a score recommendation.

Another member suggested that language surrounding the score recommendation should make it clear that transplant programs and NLRB reviewers are able to request and approve varying score recommendations to allow for consideration of extenuating circumstances.

A member stated that candidates with Budd Chiari are usually very sick and poorly represented by MELD, resulting in challenges and access to acceptable liver offers. Therefore, the member suggested that a score recommendation higher than MMaT minus three may be appropriate. Another member argued that the MELD score may be high for these candidates because there may be liver injury. A member stated that the Subcommittee can use MMaT minus three as a starting point and then review the upcoming data report to help inform whether that score recommendation should be adjusted higher or lower.

The Subcommittee discussed how score recommendations would be adjusted within a continuous distribution system.

Members pointed out that the criterion for “documentation that extrahepatic malignancy has been ruled out” is vague. A member stated that this should be clarified as they do not want transplant programs or NLRB reviewers to interpret the criterion as necessitating a bone marrow biopsy.

Next steps:

Updating NLRB Guidance

The small groups will continue to report out during the upcoming Subcommittee meetings.

CEUS & LI-RADS Alignment

The Subcommittee will continue to refine the policy language modifications to align with the intent of adding CEUS and LI-RADS 5. They will then review the final language and system requirements prior to Committee review and vote.

Upcoming Meetings

- August 22, 2024

Attendance

- **Subcommittee Members**
 - Aaron Ahearn
 - Allison Kwong
 - Chris Sonnenday
 - Erin Maynard
 - Joseph DiNorcia
 - Michael Kriss
 - Neil Shah
 - Scott Biggins
- **HRSA Representatives**
 - Jim Bowman
- **SRTR Staff**
 - Katie Audette
- **UNOS Staff**
 - Ben Schumacher
 - Jesse Howell
 - Meghan McDermott
 - Niyati Upadhyay