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Briefing to the OPTN Board of Directors on

Updates to National Liver Review Board (NLRB) Guidance & Further Alignment with Liver Imaging Reporting and Data System (LI-RADS®)

OPTN Liver & Intestinal Organ Transplantation Committee

Prepared by: Meghan McDermott
UNOS Policy Department

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OPTN

Updates to National Liver Review Board (NLRB) Guidance & Further Alignment with Liver Imaging Reporting and Data System (LI-RADS®)

Affected Policies:	*9.5.I: Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions*
Affected Guidance:	*Guidance to Liver Transplant Programs and the National Liver Review Board for Adult MELD Exceptions for Transplant Oncology* *Guidance to Liver Transplant Programs and the National Liver Review Board for Adult MELD Exception Review* *National Liver Review Board Operational Guidelines*
Sponsoring Committee:	*Liver & Intestinal Organ Transplantation*
Public Comment Period:	*January 21, 2025-March 19, 2025*
Board of Directors Meeting:	*June 9-10, 2025*

Executive Summary

The purpose of the National Liver Review Board (NLRB) is to provide equitable access to transplant for liver transplant candidates whose calculated model for end-stage liver disease (MELD) score or pediatric end-stage liver disease (PELD) score does not accurately reflect the candidate's medical urgency for transplant.[1] Since implementation, the OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) has regularly evaluated the NLRB to identify opportunities for improvement.

This proposal includes updates to the Adult MELD Exception Review and Adult Transplant Oncology Exception Review guidance documents to promote relevancy, accuracy, and consistent review of non-standard exception requests. Score recommendations for diagnoses are also added to provide a more consistent request and approval process for exceptions. The NLRB Operational Guidelines are updated to ensure that review boards reflect appropriate expertise.

Additionally, this proposal includes modifications to Hepatocellular Carcinoma (HCC) policy and guidance to add contrast-enhanced ultrasound (CEUS) as an acceptable diagnostic tool for standard HCC exceptions. Proposed changes also align imaging classification criteria to the Liver Imaging Reporting and Data System (LI-RADS®)[2] terminology in *Policy 9.5.I: Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions.*

Public comment was supportive of the proposed modifications. Given the broad support for NLRB guidance document updates, the Committee only made minor post-public comment changes for

[1] *Proposal to Establish a National Liver Review Board*, OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, https://optn.transplant.hrsa.gov/ (accessed May, 16, 2025).
[2] American College of Radiology: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS.

consistency and clarification. While there was strong support for incorporating CEUS into HCC policy, public comment emphasized the importance of allowing CEUS to be used as an independent diagnosis tool for HCC which the Committee has adjusted post-public comment.

Purpose

The purpose of this proposal is to continue to improve the National Liver Review Board (NLRB) by creating a more efficient and equitable system for reviewing Model for End-Stage Liver Disease (MELD) and Pediatric End-Stage Liver Disease Model (PELD) exception requests. This proposal includes several changes to the NLRB guidance documents that seek to update content for accuracy and relevancy as well as provide non-standard exception MELD and PELD score recommendations for diagnoses to ensure more equitable access to transplant through non-standard exceptions. NLRB Operational Guidelines updates are included to ensure that review boards reflect appropriate expertise.[3] Additionally, the Committee is proposing modifications to Hepatocellular Carcinoma (HCC) policy and guidance to add contrast-enhanced ultrasound (CEUS) as an acceptable diagnostic tool for standard HCC exceptions and align imaging classification criteria to liver imaging reporting and data system (LI-RADS) terminology in *Policy 9.5.I: Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions.*

Background

National Liver Review Board

When being listed for a liver transplant, candidates receive a calculated MELD or PELD score, which is based on a combination of the candidate's clinical lab values.[4] These scores are designed to reflect the probability of death on the waitlist within a 90-day period, with higher scores indicating a higher probability of mortality and increased urgency for transplant. Candidates who are less than 12 years old receive a PELD score, while candidates who are at least 12 years old receive a MELD score. Candidates that are particularly urgent are assigned Status 1A or 1B.

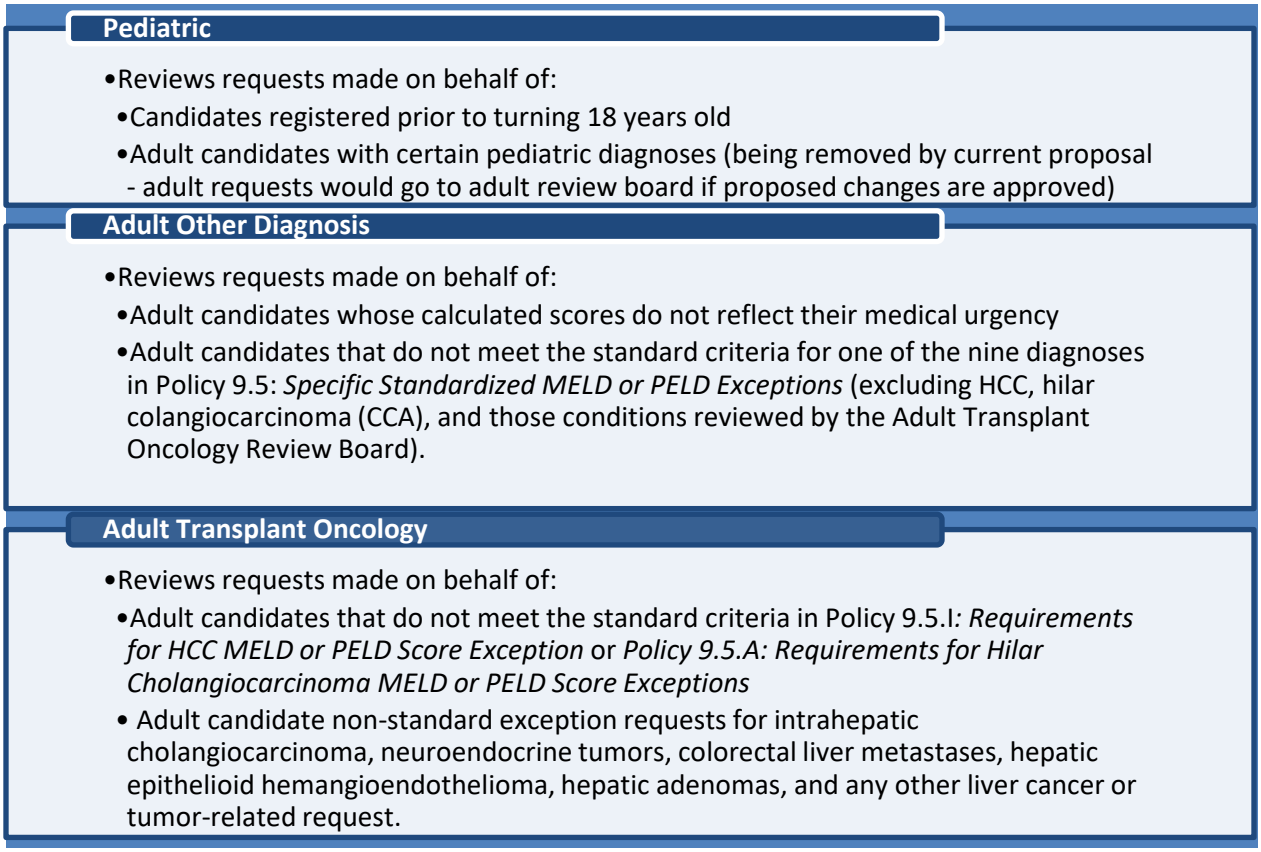
When a transplant program believes that a candidate's calculated MELD or PELD score does not accurately reflect a candidate's medical urgency, they can request a score exception. The NLRB is responsible for reviewing non-standard exception requests and either approving or denying the requested score. The NLRB was approved by the OPTN Board of Directors (the Board) during a June 2017 meeting and was implemented on May 14, 2019.[5]

Under the NLRB, candidates who meet the criteria outlined in OPTN policy for one of the nine standardized diagnoses are eligible to have their exception automatically approved without review by the NLRB.[6] If a candidate does not meet the standardized criteria in OPTN policy or is seeking an exception outside of one of the nine diagnoses in policy, a non-standard exception request can be submitted to the NLRB.

[3] The proposal submitted for public comment noted some language updates to the NLRB Operational Guidelines. However, these language updates were included as part of the *National Liver Review Board (NLRB) Updates Related to Transplant Oncology* proposal (Board approved 2024) which was implemented during this proposal's public comment period. Therefore, changes to the NLRB Operational Guidelines have been updated to reflect the current version.
[4] The calculations for the MELD and PELD scores can be found in *OPTN Policy 9.1 D and 9.1 E.* Available at https://optn.transplant.hrsa.gov/.
[5] *Proposal to Establish a National Liver Review Board*, OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, https://optn.transplant.hrsa.gov/ (accessed May, 16, 2025).
[6] OPTN Policy 9.5, *Specific Standardized MELD or PELD Exceptions* (May 16, 2025).

There are three specialty review boards: Pediatric, Adult Other Diagnosis, and Adult Transplant Oncology (**Figure 1**). Each specialty review board has an associated guidance document.[7]

Figure 1: National Liver Review Board: Specialty Review Boards



The guidance documents contain information for review board members and transplant programs on diagnoses and clinical situations not included as one of the standardized diagnoses in policy. They provide recommendations on which candidates should be considered for a MELD or PELD exception and are based on published research, clinical guidelines, medical experience, and data. The documents are intended to help ensure consistent and equitable review of non-standard exception cases and are not OPTN policy.

Because the guidance documents are consulted by transplant programs and NLRB reviewers when applying for and reviewing non-standard exception requests, they impact which liver candidates are approved for a MELD or PELD exception. Therefore, it is necessary for the Committee to update the guidance documents periodically to ensure they continue to align with current clinical consensus and updated data.

[7] NLRB Guidance Documents are available at https://optn.transplant.hrsa.gov/about/review-boards/#LiverReviewBoard.

HCC Diagnostic Tools & Imaging Criteria

Additionally, OPTN *Policy 9.5.I: Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions* outlines specific criteria that candidates must meet to be approved for a standard HCC exception. Ensuring this policy remains up to date with current practice promotes access and helps make the NLRB more efficient by having more exceptions automatically approved. This proposal includes updates to *Policy 9.5.I* on acceptable diagnostic imaging for HCC. The changes align OPTN policy with the LI-RADS criteria which is developed by the American College of Radiology (ACR). ACR provided requested subject matter expertise in the development of this proposal.

Proposal for Board Consideration

The Committee proposes updates to the NLRB's "Adult MELD Exception Review" and "Adult MELD Exceptions for Transplant Oncology" guidance documents to ensure relevancy, accuracy, and consistency. As part of an ongoing effort, modifications to these guidance documents ensure that the guidance for transplant programs and NLRB reviewers are based on current literature and practice, as well as provide clear recommendations.

The Committee decided that score recommendations should be provided for each diagnosis in the guidance documents. Currently, only five diagnoses in the adult guidance have associated score recommendations. Recent data shows that the median score for non-standard exceptions approved for the 13 conditions considered as part of this proposal was Median MELD score at transplant (MMaT)-3.[8]

The Committee recommends that non-standard exceptions for conditions without a current score recommendation should be approved for MMaT-3 or MMaT for more severe conditions.[9] This aims to create a more consistent request and approval process for non-standard exceptions. This is also consistent with the standardized exceptions currently in policy.

The goal of providing score recommendations for all diagnoses is to align with the conditions that already have score recommendations and to reduce significant differences in scores approved for exceptions by reviewers, especially for candidates with the same condition.

Most exception score recommendations are based on the donor hospital's MMaT. Therefore, MELD exception scores may vary based on liver offers from different donor hospitals, and the specific scores will not be known until the match is run.[10] The exact exception scores will be assigned based on the MMaT of transplants performed within 150 nautical miles (NM) of the donor hospital where the match is being run. The Committee's intent is to provide non-standard exception scores that give candidates the appropriate priority points based on transplants performed near the donor hospital. Using MMaT ensures that a candidate receives an appropriate score relative to other candidates' MELD scores in a

[8] OPTN Descriptive Data Request. "Non-Standard Exception Score Recommendation Data Request." Prepared for OPTN Liver and Intestinal Organ Transplantation Committee's NLRB Subcommittee Conference Call, September 26, 2024.
[9] Meeting Summary for September 26, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[10] Frequently Asked Questions: Calculate Median MELD at Transplant (MMaT) around the Donor Hospital and Update Sorting within Liver Allocation. Available at https://optn.transplant.hrsa.gov/media/amdkjmg0/1379-faq-mmat-at-donor-hospital-sorting-changes.pdf.

specific area, ensuring that the sickest candidates, with high MELD scores, receive the highest medical urgency.

The Committee plans to closely monitor the impact of these score recommendations and adjust them as needed in the future.

The NLRB Operational Guidelines are also updated to ensure appropriate expertise in reviewing exception requests.

Additionally, the Committee proposes updates to OPTN *Policy 9.5.I* to add CEUS as an acceptable diagnostic tool for HCC standard exceptions and to align imaging classification criteria to LI-RADS terminology. Changes to the NLRB Adult Transplant Oncology Guidance align with changes to OPTN *Policy 9.5.I.vi: Table 9-9* that aid NLRB reviewers and coordinators by describing imaging requirements for Class 5 lesions. New tables added to guidance include one detailing how HCC lesions can be classified as LI-RADS 5 [11] and another detailing criteria when submitting CEUS as an imaging option. If a lesion meets LI-RADS 5 criteria, it is definitively considered an HCC lesion. Updates to tables detailing documentation requirements for contrast-enhanced multiphase computer tomography scan (CT) or magnetic resonance imaging (MRI) of the liver are also included.

Post-public comment, the Committee made minor updates to the NLRB guidance documents. The majority of these were for consistency purposes. For the HCC policy, the Committee updated policy language to reflect public comment feedback that CEUS can be used as an independent diagnostic tool. More information on post-public comment changes are detailed in their respective sections below.

NLRB Guidance Updates

The Committee reviewed and discussed the results of public comment and concluded that only minor changes to the guidance documents were needed. The Committee noted that there were no major themes relevant from the public comment submitted.[12] Since these documents are meant to provide guidance, and not dictate medical practice, it is the sentiment of the Committee that some criteria are best left broad to lend to the autonomy of transplant program and NLRB review decision-making.

The following are modifications that were made to the guidance documents:

- Changed Hepatic Epithelioid Hemangioendothelioma guidance to state that extrahepatic disease is not a contraindication (this was the original intent of the guidance)
- Formatted the score recommendation to be consistent
- Changed “patients” to “candidates”
- Changed “>”, “≥”, “<“, “≤“ to “greater than”, “greater than or equal to”, “less than”, “less than or equal to”
- Corrected minor formatting issues and typos

[11] LI-RADS Diagnostic Criteria, American College of Radiology. https://www.acr.org/-/media/ACR/Files/Clinical-Resources/LIRADS/Chapter-8-LIRADS-Categories.pdf.
[12] Meeting Summary for April 4, 2025, OPTN Liver & Intestinal Organ Transplantation Committee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).

Adult Meld Exception Review Guidance

Budd Chiari

Budd Chiari is a medical condition characterized by hepatic vein thrombosis.[13] Candidates with Budd Chiari may present with evidence of decompensated portal hypertension (ascites and hepatic hydrothorax), among other symptoms.

The current MELD exception guidance for Budd Chiari requires that transplant programs submit the following documentation for review by the NLRB:

- Failed medical or surgical management (specify)
- Any contraindications to Transjugular Intrahepatic Portosystemic Shunt (TIPS) or TIPS failure; specify
- Documentation that extrahepatic malignancy has been ruled out

The Committee proposes a specific score recommendation of MMaT-3, replacing a recommendation to consider approval of exception points, but without a recommended score.[14]

Hepatic Hydrothorax

Hepatic hydrothorax is the excessive accumulation of transudate in the pleural cavity in candidates with decompensated liver cirrhosis (LC) but without cardiopulmonary and pleural diseases.[15]

The current MELD exception guidance for Hepatic Hydrothorax requires that transplant programs submit the following documentation for review by the NLRB:

- At least 1 thoracentesis over 1 liter (L) weekly in last 4 weeks; report date and volume of each thoracentesis
- Pleural fluid is transudative by pleural albumin-serum albumin gradient of at least 1.1 g/dL and by cell count
- No evidence of heart failure; provide objective evidence excluding heart failure
- Pleural fluid culture negative on 2 separate occasions
- Pleural fluid cytology is benign on 2 separate occasions
- There is contraindication to TIPS; specify contraindication
- Diuretic refractory

The Committee proposes reducing the requirement for pleural fluid documentation from two instances to one for both negative culture and benign cytology. This change maintains the rigor of initial diagnostic testing while easing the documentation burden for ongoing exceptions. For thoracentesis, the Committee recommends documenting at least 1 liter of pleural fluid removal on four separate occasions within the last 4-6 weeks. Transplant programs must record the date and volume of each removal. If a drainage catheter is used, a medical provider or registered nurse (RN) must perform or witness the documentation.

Per American Society for the Association of Liver Diseases (AASLD) guidelines, TIPS placement in candidates with MELD scores as low as 18 in some studies and more clearly with MELD scores above 21 carries a higher mortality risk. The benefit of TIPS in hydrothorax is closely related to liver function and

[13] National Institutes of Health: https://pmc.ncbi.nlm.nih.gov/articles/PMC4147117/.
[14] Meeting Summary for July 25, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[15] Garbuzenko DV, Arefyev NO. Hepatic hydrothorax: An update and review of the literature. World J Hepatol. 2017 Nov 8;9(31):1197-1204. doi: 10.4254/wjh.v9.i31.1197. PMID: 29152039; PMCID: PMC5680207.

age.[16] Therefore, the Committee decided that TIPS is not a requirement but rather should remain in background information because TIPS cannot always be performed.

The Committee recommends that candidates meeting these criteria are eligible for a MELD exception score of MMaT-3.

Hereditary Hemorrhagic Telangiectasia

Hereditary hemorrhagic telangiectasia (HHT) is an uncommon, autosomal dominant genetic disorder characterized by mucocutaneous telangiectasias, as well as arteriovenous (AV) malformations in the brain, spine, lungs, gastrointestinal tract, and liver.[17]

Case review for HHT currently requires documentation of high output cardiac failure by echocardiography and imaging supporting intra-hepatic AV malformations or severe diffuse bilobar hepatic necrosis in the setting of hepatic AV malformation.

The Committee added right heart catheterization as an option for case documentation and a requirement for documentation of symptoms of heart failure. The Committee proposed a two-tier approach for determining priority points based on the American Heart Association classification of heart failure.[18] This two-tier approach has candidates who met the criteria for this exception eligible for MMaT-3 and candidates who additionally have severe ongoing complications of heart failure eligible for MMaT.

The proposed MELD exception guidance for HHT requires that transplant programs submit the following documentation for review by the NLRB:

- Documentation of high output cardiac failure by echocardiography or right heart catheterization, and symptoms of heart failure
- Imaging supporting intra-hepatic arteriovenous (AV) malformations or severe diffuse bilobar hepatic necrosis in the setting of hepatic AV malformation

The Committee proposes that candidates who meet the criteria above should be eligible for a MELD exception score equivalent to MMaT-3. After discussing different classes of heart failure, The Committee felt that severe ongoing complications of heart failure may warrant MMaT.

Polycystic Liver Disease

Polycystic Liver Disease (PLD) is characterized by the progressive growth of cysts of various sizes scattered throughout the liver.[19]

The Committee clarified that the guidance applies to candidates with PLD who failed medical or surgical management, and removed the reference to clinical eligibility for resection/fenestration or alternative

[16] Lee, Edward Wolfgang[1]; Eghtesad, Bijan[2]; Garcia-Tsao, Guadalupe[3,4]; Haskal, Ziv J.[5]; Hernandez-Gea, Virginia[6]; Jalaeian, Hamed[7]; Kalva, Sanjeeva P.[8]; Mohanty, Arpan[9]; Thabut, Dominique[10]; Abraldes, Juan G.[11]. AASLD Practice Guidance on the use of TIPS, variceal embolization, and retrograde transvenous obliteration in the management of variceal hemorrhage. Hepatology 79(1):p 224-250, January 2024. | DOI: 10.1097/HEP.0000000000000530.

[17] National Institutes of Health. https://medlineplus.gov/genetics/condition/hereditary-hemorrhagic-telangiectasia/.

[18] Meeting Summary for September 26, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).

[19] National Organization for Rare Diseases. https://rarediseases.org/rare-diseases/polycystic-liver-disease/.

therapy since the change in language is more direct and comprehensive.[20] PLD candidates are recommended for MMaT in current guidance. This current score recommendation is not proposed for change.

Portopulmonary Hypertension

Portopulmonary hypertension (POPH) is a form of pulmonary arterial hypertension (PAH) associated with portal hypertension with or without underlying chronic liver disease.[21]

This condition is addressed as a standard exception in policy in *Policy 9.5.G: Requirements for Portopulmonary Hypertension MELD or PELD Score Exceptions*, so the Committee considered that it should be removed from guidance.[22] While the condition could be left in guidance as a reference point to direct readers back to policy, the Committee decided to remove it since they agreed it did not need to exist in both policy and guidance.[23]

Primary Sclerosing Cholangitis and Secondary Sclerosing Cholangitis

Primary Sclerosing Cholangitis (PSC) is a chronic liver disease affecting the bile ducts.[24]

The Committee proposes to separate this guidance into two sections based on the severity of a candidate's condition. The Committee discussed that candidates who do not have cirrhosis may need a different MELD exception than those with severe cholangitis, with preference given to those with underlying cirrhosis. The Committee's intention is to make it easier for candidates with this condition to receive an exception because of the benefit**.**[25] Less extreme cases of Sclerosing Cholangitis are recommended for MMaT-3, and severe cases are recommended for MMaT.[26] The Committee reviewed waitlist drop out data for these conditions to inform their decision.[27] The language is similar to the exception guidance for Ischemic Cholangiopathy, because both conditions include an increased bile stricture which is not responsive to treatment.

The proposed, separated guidance is as follows:

Candidates who meet the following criteria are eligible for a MELD exception equivalent to MMaT-3:

- The candidate has been admitted to the hospital two or more times within a one-year period with either of the following:
    - Documented blood stream infection
    - Evidence of sepsis with hemodynamic instability requiring vasopressors

[20] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025)./.
[21] Saleemi, Sarfraz. Portopulmonary hypertension. Annals of Thoracic Medicine 5(1):p 5-9, Jan–Mar 2010. | DOI: 10.4103/1817-1737.58953.
[22] Meeting Summary for March 12, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[23] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[24] National Institutes of Health. https://www.niddk.nih.gov/health-information/liver-disease/primary-sclerosing-cholangitis#:~:text=Print%20All%20Sections-,Definition%20%26%20Facts,and%20causes%20further%20liver%20damage.
[25] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[26] Ibid.
[27] David Goldberg et al., "Waitlist Survival of Patients with Primary Sclerosing Cholangitis in the Model for End-Stage Liver Disease Era," Liver Transplantation 17, no. 11 (October 26, 2011): 1355–63, https://doi.org/10.1002/lt.22396.

In addition, candidates are eligible for a MELD exception equivalent to MMaT if they meet at least two of following criteria:

- The candidate has a biliary tract stricture(s) which are not responsive to treatment by interventional radiology (i.e. PTC) or therapeutic endoscopy (ERCP/EUS).
- The candidate has been diagnosed with a high-resistant infectious organism (e.g. Vancomycin Resistant Enterococcus (VRE), Extended Spectrum Beta-Lactamase (ESBL) producing gram-negative organism, Carbapenem-resistant Enterobacteriaceae (CRE) and Multi-drug resistant Acinetobacter).
- The candidate has cirrhosis.

Metabolic Disease

Metabolic Disease is rare, and is mainly a pediatric condition, although some adult cases have been considered for exception. Since the clinical presentation of metabolic disease can vary so much, the guidance for exception is intentionally left to be considered more liberally.

The Committee added a recommendation for MMaT-3 for metabolic disease candidates with mild symptoms and acknowledgement that a higher exception score may be warranted for candidates with life threatening complications.[28]

After coming up with the score recommendations, the Committee also included guidance that candidates with life threatening complications may be considered for an increased priority score. This ensures the guidance preserves the possibility for higher exception scores when warranted.

No other changes, besides the scoring recommendation, are proposed.

Post-transplant complications: Early Allograft Dysfunction (Small for Size)

Small for size syndrome (SFSS) is a clinical syndrome caused by the transplantation of a liver graft that is too small for a recipient.

The Committee proposed a score-based grade of SFSS in guidance for non-standard exceptions that estimated the degree of allograft dysfunction and is based on recently published consensus guidelines.[29]

To clarify the diagnosis, the Committee now specifically requests the allograft anatomy, defined allograft risk factors for small for size syndrome, as well as any intraoperative or postoperative interventions used for treatment. These details are requested but not required to receive exception points.

The Committee now offers the following guidance, defining the necessary disease severity for MELD exception: For most candidates, the calculated MELD score will provide adequate priority, but candidates with severe allograft dysfunction (Grade C) [30] have excess mortality justifying an exception score of MMaT.[31]

The Committee considered including Grade B[32] SFSS with certain conditions as qualifying for the exception as well. However, they determined that any candidate with Grade B SFSS would likely have a

[28] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[29] Meeting Summary for September 26 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[30] Grade C is a total Bilirubin >10 mg/dl and international normalized ratio (INR) > 1.6 at day 7 OR total bilirubin >20 at day 14.
[31] A. Kow et al. Transplantation. October 2023; Vol. 107:2226-37.
[32] Grade B is Day 7 Total Bilirubin >10 mg/dL or INR >1.6, Day 14 Total Bilirubin >10mg/dL and ascites IL/d.

high enough MELD score to reflect their expected waitlist mortality without warranting additional priority. As a result, Grade B SFSS is not included as qualifying for additional priority.

The Committee felt that Small for Size was not a clear term. The Committee decided to rename this guidance Early Allograft Dysfunction (EAD) in Reduced Size Livers (Small for Size Syndrome). Small for Size Syndrome is considered outdated nomenclature. Changing the title and keeping Small for Size Syndrome in parentheses with a more accurate term (Early Allograft Dysfunction) improves clarity.

The Committee proposes the following guidance for Early Allograft Dysfunction (Small for Size):

Living donor allografts, split allografts, and reduced size allografts are prone to early allograft dysfunction secondary to elevated portal flow or pressure. Symptoms should develop less than 30 days following transplantation without other identified cause of graft dysfunction such as vascular thrombosis, prolonged ischemia, or other etiology.

Key Risk factors include:

- Graft to Recipient Weight Ratio (GRWR) < 0.8%
- Graft Volume to Standard Liver Volume ratio of <40%
- Portal Pressure > 15 mm hg or portal cava gradients >10 mm Hg
- Portal flow > 250ml/min/100gm graft weight

Documentation submitted for case review should include the anatomy of the split allograft, the above risk factors for small for size syndrome, and any intraoperative or postoperative interventions used for treatment.

In most cases, the calculated MELD score will provide adequate priority. Candidates with severe allograft dysfunction classified as Grade C are proposed to be eligible for MMaT due to the severity of disease and risk of mortality.

Post-transplant complications: Diffuse Ischemic Cholangiopathy and Late Vascular Complications

Committee members were concerned that the criteria in Late Vascular Complications related to ischemic cholangiopathy are different than the NLRB guidance section for ischemic cholangiopathy, so they decided to combine the two separate sections into one section to streamline guidance.[33,34]

Diffuse ischemic cholangiopathy is a complication typically associated with donation after cardiac death (DCD) liver transplant, but the Committee combined and revised the two sections since this condition occurs in livers besides DCD, including Donation after Brain Death (DBD).[35]

Late vascular complications are biliary which indicates they would fall into one of the other exception pathways. The Committee agreed that a sentence could be added to the ischemic cholangiopathy section that states that a cause of ischemic cholangiopathy could be a late vascular complication and those candidates could apply for an exception. Candidates with both conditions likely have similar waitlist mortalities and warrant similar exception scores.

[33] Meeting Summary for October 9, 2024, OPTN Liver & Intestinal Organ Transplantation Committee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[34] Meeting Summary for August 22, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[35] Meeting Summary for October 9, 2024, OPTN Liver & Intestinal Organ Transplantation Committee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).

Proposed guidance is updated to be more specific and to indicate what long-term morbidity means with this condition. Updated, combined guidance criteria include documentation of:

1. Risk factor(s) for ischemic cholangiopathy (e.g. hepatic artery thrombosis post-transplant or DCD donor characteristics)
2. Evidence of ischemic cholangiopathy and non-anastomotic biliary stricture, including two or more of the following criteria within 12 months of transplant:
    - Persistent cholestasis as defined by abnormal bilirubin (greater than 2 mg/dl) for greater than 4 weeks
    - Evidence of severe infection, such as:
        - Two or more episodes of cholangitis with an associated bacteremia requiring hospital admission.
        - Repeated multidrug-resistant bacteremia
        - Abscesses and/or biliary strictures requiring frequent interventions (e.g. percutaneous transhepatic biliary drainage (PTBD), endoscopic retrograde cholangiopancreatography (ERCP) requiring at least two documented readmissions over 6 months.

The Committee recommends that candidates may be considered for MELD exception score of MMaT-3.

Adult Transplant Oncology Guidance

Hepatocellular Carcinoma (HCC)

This section includes updates to diagnostic imaging tables to provide specific evaluation criteria in one location for reviewers to determine exceptions. Updates include:

- Addition of a table including the most recent LI-RADS 5 criteria[36]
- Updated imaging requirements for both multiphase CT and MRI
- Addition of a table to list the imaging requirements for the CEUS imaging option to submit a standard exception request for HCC

Neuroendocrine Tumors (NET)

The Committee reviewed guidance for NET.[37] Current criteria for exception requests include resection of primary malignancy and extra-hepatic disease without any evidence of recurrence for at least six months prior to MELD exception request and evidence of Neuroendocrine Liver Metastasis (NLM) limited to the liver, bi-lobar, and not amenable to resection. Additionally, documentation of radiological characteristics by either CT or MRI are required for exception.

The Committee decided to remove bi-lobar, or two distinct and separate lesions, from criteria for MELD exception points.[38] They decided to remove content about MRI or CT scan characteristics and instead base guidance on Positron Emission Tomography (PET) scan with dotatate or liver biopsy if the PET scan is unclear. The Committee agreed that most transplant programs do not detect NET with a CT or an MRI,

[36] American College of Radiology: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/LIRADS/Chapter-8-LIRADS-Categories.pdf.
[37] Meeting Summary for September 26 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[38] Mazzaferro V, Pulvirenti A, Coppa J. Neuroendocrine tumors metastatic to the liver: how to select patients for liver transplantation? *Journal of Hepatology*, Oct 2007; 47(4): 460-6.

and most transplant programs do have a version of a PET. The Committee agreed that NET is now detected most of the time with PET dotatate. The Committee also removed language stating that some neuroendocrine tumors located in specific areas did not qualify for automatic MELD exception. The language was removed to clarify that there are no automatic exception points associated with NLRB guidance.

The Committee agreed that language can be added to use either the primary lesion or a resected lesion to differentiate between a Grade 1 or a Grade 2 tumor, since this cannot always be determined with the primary lesion and it is sometimes not available. The Committee also discussed if Grade 1 or Grade 2 tumors should continue to be differentiated using the mitotic rate of less than 20 per 10 hepatopulmonary fusion (HPF) with a Ki-67 index of less than 20 percent. They decided to keep this method of differentiation since there is no new data demonstrating otherwise.[39]

While this same literature, referred to as the "Mazzaferro Milan Criteria," supports the criteria that metastatic liver volume should not exceed fifty percent to qualify for this exception, the Committee decided to remove the requirement because they felt that fifty percent was not measurable.

The score recommendation proposed by the Committee is MMaT-3.

Hepatic Epithelioid Hemangioendothelioma (HEHE)

HEHE is a rare, low grade primary liver tumor of mesenchymal cell origin.[40]

The current MELD exception guidance for HEHE requests transplant programs to perform a biopsy to establish the diagnosis of HEHE and exclude hemangiosarcoma.

Based on the review of recent literature, the Committee discussed that HEHE recurs over years and should not impact early post-transplant outcomes.[41] The Committee agreed that a statement regarding the data detailing the impact of microvascular invasion should be removed from guidance, as the data is no longer accurate.[42] The Committee also agreed that the NLRB guidance should not include educational statements or comments as written in current guidance, but should only outline criteria for non-standard exceptions.

The Committee proposes updating this guidance to include, in addition to a biopsy, meeting the following criteria:

- Biopsy proven diagnosis of HEHE and exclude hemangiosarcoma.
- Absence of macrovascular invasion on biopsy or imaging.
- Lesions are unresectable.

[39] Mazzaferro V, Pulvirenti A, Coppa J. Neuroendocrine tumors metastatic to the liver: how to select patients for liver transplantation? *Journal of Hepatology*, Oct 2007; 47(4): 460-6.
[40] Kou K, Chen YG, Zhou JP, Sun XD, Sun DW, Li SX, Lv GY. Hepatic epithelioid hemangioendothelioma: Update on diagnosis and therapy. World J Clin Cases. 2020 Sep 26;8(18):3978-3987. doi: 10.12998/wjcc.v8.i18.3978. PMID: 33024754; PMCID: PMC7520791.
[41] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[42] Lerut, J.P., G. Orlando, R. Adam, et al. "The place of liver transplantation in the treatment of hepatic epitheloid hemangioendothelioma: report of the European liver transplant registry." Ann Surg 246 (2007): 949-57.

The criteria are based on recent publications. Additionally, data shows that candidates with multiple lesions have a high post-transplant survival rate, so the committee included a requirement that the lesions be unresectable to qualify for an exception.[43]

The Committee additionally added a score recommendation of MMaT-3.

Hepatic Adenomas (HA)

HA are rare benign nodules occurring principally in women taking oral contraceptives.[44] The two types of hepatic adenomas are solitary and adenomatosis, resulting from risk factors including exposure to estrogens, anabolic steroids, genetic syndromes such as glycogen storage disease (GSD) or Abernathy syndrome, and metabolic syndrome.[45]

The current MELD exception guidance for hepatic adenomas requires that transplant programs submit the following documentation for review by the NLRB:

- Adenoma in the presence of Glycogen Storage Disease
- Unresectable β Catenin (+) Adenoma
- Adenoma(s) with all three below:
  - Unresponsive to medical management
  - Unresectable
  - Progressive or with complication such as hemorrhage or malignant transformation (must specify)

Candidates with adenomatosis have innumerable lesions on both sides of the liver. It is difficult to know which lesion might have malignant potential because all lesions cannot be biopsied. Liver transplantation is the only definitive treatment option. Adenomatosis typically occurs in the presence of glycogen storage disease, but not always.

The Committee also considered that the number of hepatic adenoma diagnoses last year was approximately 40 and there was concern that creating more options to receive an exception may cause requests for more candidates than those who may actually need an exception. A proposed number of adenomas is included in the criteria recommendations since adenomatosis is defined as more than 10 adenomas present.

The Committee decided to request documentation of the size of an adenoma as a criterion, as larger adenomas are considered more medically concerning but wanted to continue to ensure priority is given to candidates with more severe conditions like HCC.

The Committee proposes the following changes to this guidance.[46]

- An exception can be additionally approved for an unresectable adenoma in a candidate with liver adenomatosis (>10 HA).
- If exceptions with progressive or complicated hepatic adenomas are requested, documentation must be specific to include supportive details including size.

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[43] Nudo, C.G., E.M. Yoshida, V.G. Bain, et al. “Liver transplantation for hepatic epithelioid hemangioendothelioma: the Canadian multicentre experience.” Can J Gastroenterol 22 (2008):821-4.
[44] Jean-Charles Nault et al., “Molecular Classification of Hepatocellular Adenoma in Clinical Practice,” Journal of Hepatology 67, no. 5 (2017): pp. 1074-1083, https://doi.org/10.1016/j.jhep.2017.07.009.
[45] Meeting Summary for October 24, 2024, OPTN NLRB Subcommittee, https://optn.transplant.hrsa.gov/ (accessed May 16, 2025).
[46] Ibid.

The Committee proposes that candidates who meet the criteria above should be eligible for a MELD exception score equivalent to MMaT-3.

NLRB Operational Guidelines

The Committee determined that language indicating that adult exception requests with certain pediatric conditions go to the Pediatric Review Board should be removed. This language currently directs adult exceptions requests with pediatric conditions (nonspecific) to the Pediatric Review Board. The Committee would like all adult exception requests to be submitted to adult review boards to ensure appropriate expertise in the review process. There have been a small number of exception requests for adults with metabolic disease that have been sent to the Pediatric Review Board for review.

The Committee received no public comment feedback on the proposed changes to the NLRB operational guidelines. No changes have been made post-public comment.

OPTN Policy 9.5.I: HCC Diagnostic Tools & Imaging Classification Criteria

The Committee is proposing two updates to OPTN policy to align with recommendations and terminology used by the American College of Radiology.[47] The proposed updates will allow candidates where a CEUS was used to diagnosis HCC a pathway for automatic approval of the standard HCC exception and align OPTN terminology with the terminology used by radiologists per LI-RADS standards. The proposed changes were drafted in consultation with subject matter experts that develop and maintain the LI-RADS criteria.

Numerous public comments noted that literature supports CEUS as an independent diagnostic tool for HCC and recommended modifying the policy language to allow this. The Committee proposes post-public comment changes to the policy language to align with this feedback and removed language that previously had stated CEUS was to be used as an adjunct diagnostic tool.

Contrast-Enhanced Ultrasound (CEUS)

CEUS can detect a variety of diseases and conditions by using an intravenous agent that contains microbubbles that allows for the ability to see the flow of blood through organs and blood vessels.[48] For HCC, CEUS can be used as a diagnostic tool to confirm the presence of HCC. In instances where CT or MRI show atypical imaging features, a CEUS may be used to accurately diagnosis HCC.[49]

Current OPTN policy[50] states that one criterion required prior to applying for a standardized HCC exception is that "an evaluation of the number and size of lesions before locoregional therapy that meet Class 5 criteria using a dynamic contrast-enhanced CT or MRI" must be performed. The Committee affirms that CT or MRI should be the sole imaging tools for determining the number and size of lesions but proposes that CEUS may be used as a diagnostic tool to confirm HCC diagnosis per *Policy 9.5.I.vi: Imaging Requirements for Class 5 Lesions.*

[47] American College of Radiology: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/LIRADS/Chapter-8-LIRADS-Categories.pdf.
[48] Cleveland Clinic: https://my.clevelandclinic.org/health/diagnostics/22754-contrast-enhanced-ultrasound-ceus.
[49] Fraquelli M, Nadarevic T, Colli A, Manzotti C, Giljaca V, Miletic D, Štimac D, Casazza G. Contrast-enhanced ultrasound for the diagnosis of hepatocellular carcinoma in adults with chronic liver disease. Cochrane Database Syst Rev. 2022 Sep 2;9(9):CD013483. doi: 10.1002/14651858.CD013483.pub2. PMID: 36053210; PMCID: PMC9438628.
[50] OPTN Policy 9.5.I.i: *Initial Assessment and Requirements for HCC Exception Requests,* as of September 2024.

Currently in instances where a CEUS was used to diagnosis HCC, transplant programs must submit non-standard exceptions for HCC for these candidates. Including CEUS as an acceptable diagnostic tool for determining Class 5 criteria will help standardize these situations and lessen the review of the NLRB. These proposed modifications apply to both pediatric and adult HCC populations.

Additional updates to the HCC policy and guidance include updating the terminology of "dynamic" to "multiphase" per recommendation from the American College of Radiology for use of more up-to-date terminology.

The Committee's proposal to add CEUS as an acceptable diagnostic tool for HCC requires updates to the OPTN Computer System in regard to the HCC exception form. Users must be able to select that their candidate had a CEUS, CT, or MRI. As diagnosis of the HCC is only relevant for the initial assessment and requirements for standardized HCC exception requests, CEUS will be added to the initial HCC exception form.

As noted earlier, public comment feedback recommended that policy language should be modified to allow CEUS to be used as a standalone diagnostic tool for HCC. The original proposal recommended that CEUS be utilized as an adjunct diagnostic tool, but research supports CEUS as an independent imaging modality for the diagnosis of HCC.[51] The Committee agreed with these recommendations and modified the policy language to reflect this feedback. CT or MRI continue to remain the only two imaging modality options for staging for HCC.

LI-RADS

LI-RADS was created to standardize the reporting and data collection for imaging of HCC.[52] The OPTN has previously aligned with LI-RADS terminology with the intent for the liver transplant community to use a consistent lexicon for the classification of HCC lesions. Currently *Policy 9.5.I.vi: Imaging Requirements for Class 5 Lesions* includes granular criteria for the classification of HCC. The Committee proposes certain criteria be modified to a single criterion that encompasses LI-RADS 5 instead of listing out the granular criteria that defines LI-RADS 5. The proposed changes highlight that LI-RADS 5 can be determined by CT, MRI or CEUS. These proposed modifications are detailed below in **Table 1**.

[51] Lyshchik A, Wessner CE, Bradigan K, Eisenbrey JR, Forsberg F, Yi M, Keith SW, Kono Y, Wilson SR, Medellin A, Rodgers SK, Planz V, Kamaya A, Finch L, Fetzer DT, Berzigotti A, Sidhu PS, Piscaglia F; CEUS LI-RADS Trial Group. Contrast-enhanced ultrasound liver imaging reporting and data system: clinical validation in a prospective multinational study in North America and Europe. Hepatology. 2024 Feb 1;79(2):380-391. doi: 10.1097/HEP.0000000000000558. Epub 2023 Aug 8. PMID: 37548928; PMCID: PMC11810132.

[52] American College of Radiology: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS.

Table 1: Summary of Modifications to Table 9-9

Class	Current	Proposed
NC – Not Categorizable	Incomplete or technically inadequate study due to image degradation or omission	No proposed changes
5A	Must meet *all* of the following: • Maximum diameter of at least 1 cm and less than 2 cm, as measured on late arterial or portal phase images • Nonrim arterial phase hyper-enhancement • *Either* of the following: o Non-peripheral washout o Biopsy	Must meet *all* of the following: • Maximum diameter of at least 1 cm and less than 2 cm, as measured on late arterial or portal phase images • *Either* of the following o LI-RADS 5 classification on CT, MRI, or CEUS o Biopsy
5A-g	Must meet *all* of the following: • Maximum diameter of at least 1 cm and less than 2 cm, as measured on late arterial or portal phase images • Nonrim arterial phase hyper-enhancement • Threshold growth defined as size increase of a mass by ≥ 50% in ≤ 180 days on MRI or CT	Remove classification (now included in LI-RADS 5 classification with 5A, above)
5B	Must meet *all* of the following: • Maximum diameter of at least 2 cm and less than or equal to 5 cm, as measured on late arterial or portal phase images • Nonrim arterial phase hyper-enhancement • *One* of the following: o Non-peripheral washout o Enhancing capsule o Threshold growth defined as size increase of a mass by ≥ 50% in ≤ 180 days on MRI or CT o Biopsy	Must meet *all* of the following: • Maximum diameter of at least 2 cm and less than or equal to 5 cm, as measured on late arterial or portal phase images • *Either* of the following o LI-RADS 5 classification on CT, MRI, or CEUS o Biopsy
5T	Any Class 5A, 5A-g, 5B lesion that was automatically approved upon initial request or extension and has subsequently been treated by locoregional therapy	Any Class 5A or 5B lesion that was automatically approved upon initial request or extension and has subsequently been treated by locoregional therapy

The changes should simplify the work of transplant coordinators, who currently must translate between the terms used by radiologists and the terms used by the liver transplant team. Aligning the terminology between these groups will reduce the chance of data entry error.

The Committee proposes to add a table that details the criteria for LI-RADS 5 for CT, MRI, and CEUS to the Adult Transplant Oncology NLRB guidance document for purposes of being an available resource for more information on the LI-RADS 5 definition. Additionally, this information will be available for reference in the online help documentation within the OPTN Computer System.

Public comment was supportive of the inclusion of LI-RADS terminology. The post-public comment changes made in relation to the LI-RADS modifications is to clarify that diagnosis of HCC through LI-RADS 5 classification can be made by CT, MRI, or CEUS.

Since diagnosis of HCC can now be determined from CT, MRI, or CEUS, the previously proposed 90-day timeframe for when CEUS would need to be performed in relation to CT or MRI is not necessary and as such has been removed from the proposed language. The Committee had proposed that the CEUS should be performed within 90-calendar days of when the CT or MRI was performed because of tumor growth considerations. Additionally, the Committee chose a 90-calendar day timeframe because CTs or MRIs are performed every three months for purposes of extending HCC exceptions. However, this language is removed from the final proposal due to the public comment feedback.

Overall Sentiment from Public Comment

The proposal was released for public comment from January 21, 2025 - March 19, 2025. Respondents were able to participate through virtual regional meetings, committee meetings, and a form on the OPTN website. American Society of Transplantation (AST) and American Society of Transplant Surgeons (ASTS) as well as several ultrasound and radiology societies submitted written public comments. Additional public comment feedback was received from transplant programs, individuals of the community, and the OPTN Pediatric Transplantation Committee.

Sentiment is collected on public comment proposals and is measured on a 5-point Likert scale from strongly oppose to strongly support (1-5). Generally, public comment sentiment has been supportive of this proposal. Below are graphics that illustrate the sentiment received through public comment.

The following graphics show sentiment received from regional meetings. This proposal was on the non-discussion agenda during regional meetings, but members were able to submit feedback on all public comment items via Poll Everywhere during each regional meeting. **Figure 2** shows the sentiment by region while **Figure 3** shows regional meeting sentiment by member type. [53]

[53] For Figure 2 and Figure 3, the top number represents the average sentiment score, and the bottom number in parentheses represents the total number of respondents. The size of the bar reflects the total number of respondents per region (Figure 2) or per member type (Figure 3).

Figure 2: Sentiment by Region (OPTN Regional Meetings)

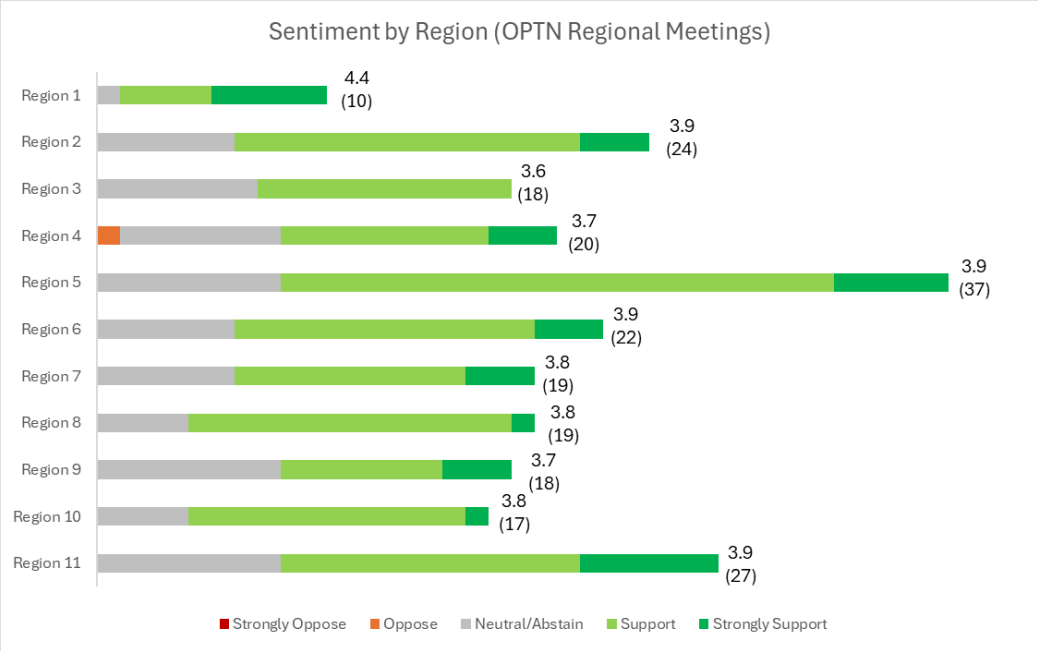


Figure 3: Sentiment by Member Type (OPTN Regional Meetings)

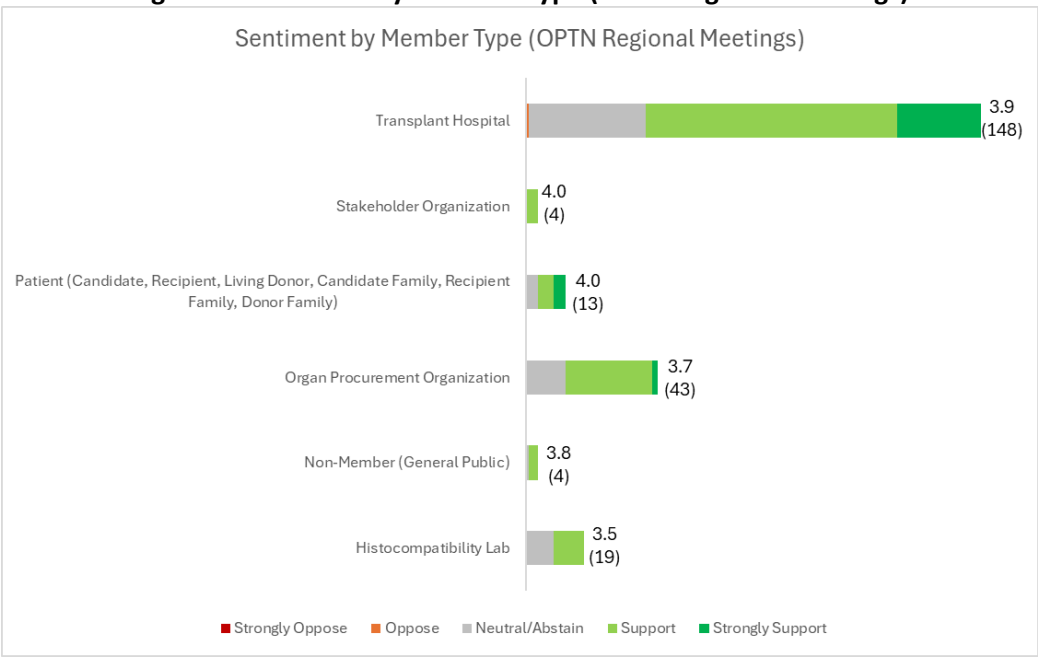


Figure 4 and **Figure 5** show the sentiment for the public comments submitted through the OPTN website which were categorized based on the sentiment expressed in the text submitted.[54] Each comment was analyzed to identify whether it conveyed support, opposition, or neutrality towards the proposal. The following definitions were used to ensure clarity and consistency in the categorization process:

- **Support:** The text of the public comment expressed a positive stance towards the proposal. Supportive comments typically contained language that endorsed, agreed with, or advocated for the proposal.
- **Do Not Support:** The text of the public comment expressed a negative stance towards the proposal. Comments that do not support the proposal contained language that opposed or disagreed with the proposal.
- **Neutral:** The text of the public comment did not clearly express a positive or negative stance towards the proposal. Neutral comments lacked definitive "support" or "not support" language or presented balanced viewpoints on the proposal.

Figure 4: Overall Support (OPTN Website Comments)

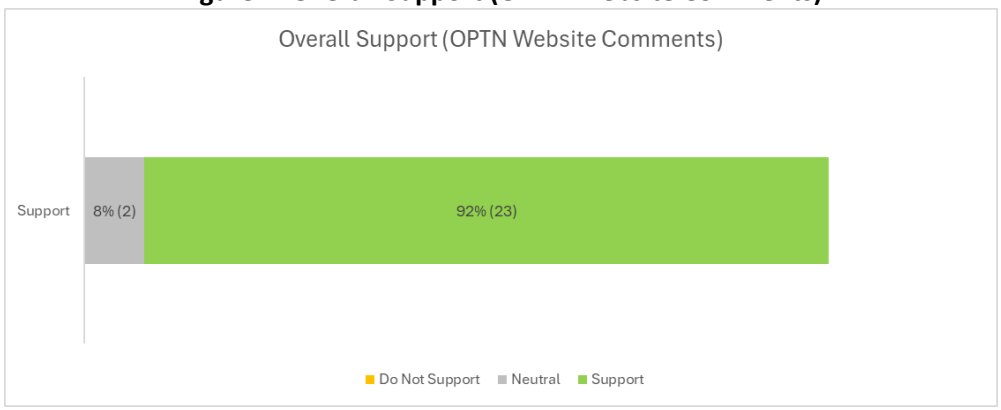
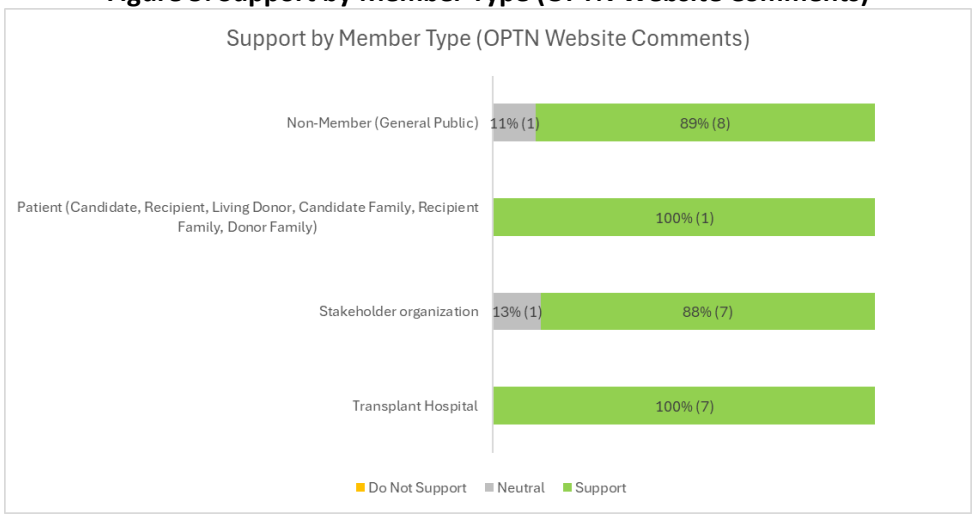


Figure 5: Support by Member Type (OPTN Website Comments)



[54] For Figure 4 and Figure 5, the number in parentheses represents the total number of comments through the OPTN website. The size of the bar reflects the total number of respondents who submitted public comment through the OPTN website (Figure 4) or by member type (Figure 5).

Overall, the transplant community and stakeholder organizations were supportive of the proposed changes to NLRB guidance and HCC policy. The majority of public comment was supportive of the proposed score recommendations and updates to NLRB guidance. As noted previously, the Committee did not identify a main theme and as such did not make any major post-public comment changes to the guidance documents. Multiple stakeholder organizations representing radiology and ultrasound experts were very supportive of the inclusion of CEUS as an acceptable diagnostic tool for HCC. Pediatric stakeholders, namely the OPTN Pediatric Transplantation Committee, Society of Pediatric Liver Transplantation (SPLT), and Society for Pediatric Radiology also supported the incorporation of CEUS as an imaging modality for the diagnosis of HCC.

Compliance Analysis

NOTA and OPTN Final Rule

This project is authorized by NOTA to establish "medical criteria for allocating organs,"[55] as well as the OPTN Final Rule, which requires the Board to establish performance goals for allocation policies, including "reducing inter-transplant program variance" in performance indicators.[56] The potential changes included in this project will ensure that transplant programs and NLRB reviewers have updated and accurate clinical guidance regarding medical criteria when submitting and reviewing exception requests. The updated guidance will assist in reducing inter-transplant program variance by facilitating a more consistent review of exception cases. By facilitating a more consistent review of exception cases, the proposal will, in turn, help ensure the equitable allocation of deceased donor organs by providing similar priority for candidates in similar clinical situations and allowing the appropriate candidates to receive a MELD or PELD exception.

OPTN Strategic Plan

This proposal seeks to improve access to transplants by 1) providing guidance on consistent score recommendations so that candidates with similar diagnoses have access to similar exception scores and 2) providing access to standard exceptions for HCC candidates who had their diagnosis confirmed by the usage of CEUS.

Implementation Considerations

Member and OPTN Operations

The proposed changes to the Adult MELD Exception Review guidance document, the Adult Transplant Oncology Exception Review guidance document, and NLRB Operational Guidelines will need to be updated on the OPTN website. It will also include updating OPTN policy 9.5.I for the modifications related to CEUS and LI-RADS. Modifications for CEUS and LI-RADS require updates to the OPTN Computer System. This will include updating initial HCC exception forms as well as associated help documentation.

The Committee discussed the need for an implementation transition plan. Upon implementation, any HCC initial case that is in pending state or submitted to the review board will remain in the current form.

[55] NOTA, 42 U.S.C. §274 (b)(2)(B).
[56] 42 C.F.R. § 121.8(b)(4).

Implemented changes will be reflected in the new HCC initial forms. Additionally, any pending or appealed metabolic adult cases submitted to the Pediatric Review Board will not convert to a different review board but will continue to be directed to the Pediatric Review Board. Transplant programs can re-submit an exception to have the Adult Other Diagnosis Review Board adjudicate the case instead.

All pending or submitted HCC exception request forms submitted for NLRB approval will remain in current state, without the additional imaging option of CEUS, to be automatically approved for a standard HCC exception. Should transplant programs want to use CEUS, they can resubmit a new HCC form.

Additionally, all pending, submitted and appealed forms for adult exception request forms that meet criteria for Metabolic Disease for NLRB approval will still be sent to the Pediatric Review Board. Should transplant programs want these cases to be reviewed by the Adult Other Diagnosis Review Board, they can withdraw their currently submitted form and file a new exception form.

Transplant Programs

Operational Considerations

Transplant programs will need to be familiar with the proposed changes to the NLRB guidance documents when submitting non-standard exception requests for liver.

Transplant programs will also need to be aware of the changes related to imaging options and LI-RADS when submitting standard HCC exceptions.

Fiscal Impact

No significant fiscal impacts were recorded for transplant hospitals.

OPTN

Operational Considerations

Relevant guidance documents will be updated. The OPTN Computer System will be updated to reflect changes to the HCC policy modifications. CEUS is proposed as an additional imaging option to diagnose a Class 5 lesion. System users will be able to input “CEUS of abdomen” and an associated imaging date in the existing section, "Imaging Study.”

The OPTN will communicate any changes prior to implementation and will provide educational resources as appropriate.

Resource Estimates

It is estimated that $162,897 will be needed to implement this proposal. Implementation would involve updates to the OPTN Computer System that include building and updating forms, modifying reporting tools, and testing to support the proposed changes. Implementation will include updating the Evaluation Plan and process documents as well as outreach to the community regarding these changes. It is estimated that $37,521 will be needed for ongoing support. Ongoing support includes member support, education, and system maintenance. In addition, ongoing support will include a monitoring report at the

6-month and 1-year timeframes. The total estimate for implementation and ongoing support is $200,418. [57]

Histocompatibility Laboratories

Operational Considerations

This proposal is not anticipated to affect the operations of histocompatibility laboratories.

Fiscal Impact

No significant fiscal impacts were recorded for histocompatibility laboratories.

Organ Procurement Organizations

Operational Considerations

This proposal is not anticipated to affect the operations of organ procurement organizations.

Fiscal Impact

No significant fiscal impacts were recorded for OPOs.

Post-implementation Monitoring

Member Compliance

This proposal will not change the current routine monitoring of OPTN members. During routine transplant hospital site surveys, the OPTN will continue to review of a sample of medical records, and any material incorporated into the medical record by reference, for documentation that data reported through the OPTN Computer System are consistent with source documentation, including completion of the required imaging.

Policy Evaluation

These data modifications will be formally evaluated approximately 6 months and 1 year post-implementation. The following metrics, and any others subsequently requested by the Committee, will be evaluated as data become available (appropriate lags will be applied, per typical OPTN conventions, to account for time delay in institutions reporting data to the OPTN Computer System) and compared to an appropriate pre-implementation cohort:

- Count and percent of standard HCC exceptions by imaging modality (CT, MRI, and Other pre-policy; CT, MRI, Contrast-Enhanced Ultrasound (CEUS), and Other post-policy)
    - Overall and stratified by OPTN Region

[57] Resource estimates are calculated by the current contractor for that contractor to perform the work. Estimates are subject to change depending on a number of factors, including which OPTN contractor(s) will be performing the work, if the project is ultimately approved.

- Count of exception forms submitted and distribution of medical urgency scores requested relative to median MELD or PELD at transplant (MMaT) by exception diagnosis
    - Overall and stratified by form type (initial, extension), outcome (approved, denied) and OPTN Region

Conclusion

This proposal updates guidance for transplant programs to submit non-standard exceptions for candidates diagnosed with liver cancers, tumors, and other conditions listed in the NLRB Adult Transplant Oncology guidance document and the Adult Other Diagnoses guidance document. The NLRB Operational Guidelines are updated to align to NLRB guidance changes proposed here.

Additionally, this proposal includes modifications to HCC policy and guidance to add CEUS as an acceptable diagnostic tool for standard HCC exceptions. This imaging classification criteria is also aligned to LI-RADS terminology in policy.

The proposed changes will update NLRB guidance for accuracy and relevancy. Reviewers will be more equipped to consistently analyze and score cases and make decisions based on their clinical expertise. Adding CEUS as an acceptable diagnostic tool for HCC exceptions provides an expanded way for candidates to receive automatic standard exception requests.

Public comment was supportive of these proposed modifications. Given the broad support for NLRB guidance document updates, the Committee only made minor post-public comment changes for consistency and clarification. While there was strong support for incorporating CEUS into HCC policy, public comment emphasized the importance of allowing CEUS to be used as an independent diagnosis tool for HCC which the Committee has adjusted post-public comment in the proposed policy language.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

9.5.I Requirements for Hepatocellular Carcinoma (HCC) MELD or PELD Score Exceptions

Upon submission of the first exception request, a candidate with hepatocellular carcinoma (HCC) will receive a score according to *Policy 9.5.I.vii: Extensions of HCC Exceptions* if the candidate meets the criteria according to *Policies 9.5.I.i through 9.5.I.vi.*

9.5.I.i Initial Assessment and Requirements for HCC Exception Requests

Prior to applying for a standardized MELD or PELD exception, the candidate must undergo a thorough assessment that includes *all* of the following:

1. An evaluation of the number and size of lesions ~~before locoregional therapy~~ using multiphase contrast-enhanced computer tomography (CT) or magnetic resonance imaging (MRI) before locoregional therapy.
2. An evaluation that the lesions ~~that~~ meet Class 5 criteria according to *Table 9-9* using a ~~dynamic~~ multiphase contrast-enhanced ~~computed tomography (~~CT~~), or (~~MRI~~)~~, or ultrasound (CEUS).
3. A CT of the chest to rule out metastatic disease. This is only required prior to applying for an initial exception. A CT of the chest is not required for exception extensions.
4. A CT or MRI to rule out any other sites of extrahepatic spread or macrovascular involvement
5. An indication that the candidate is not eligible for resection
6. An indication whether the candidate has undergone locoregional therapy
7. The candidate's alpha-fetoprotein (AFP) level

The transplant hospital must maintain documentation of the radiologic images and assessments of all OPTN Class 5 lesions in the candidate's medical record. If growth criteria are used to classify a lesion as HCC, the radiology report must contain the prior and current dates of imaging, type of imaging, and measurements of the lesion.

For those candidates who receive a liver transplant while receiving additional priority under the HCC exception criteria, the transplant hospital must submit the *Post-Transplant Explant Pathology Form* to the OPTN within 60 days of transplant. If the *Post-Transplant Explant Pathology Form* does not show evidence of HCC or liver-directed therapy for HCC, the transplant program must also submit documentation or imaging studies confirming HCC at the time of assignment.

The Liver and Intestinal Organ Transplantation Committee will review the submitted documentation or imaging studies when more than 10 percent of the *Post-Transplant Explant Pathology Forms* submitted by a transplant program in a one year period do not show evidence of HCC or liver-directed therapy for HCC.

9.5.I.ii Eligible Candidates Definition of T2 Stage

Candidates with hepatic lesions that meet T2 stage are eligible for a standardized MELD or PELD exception if they have an alpha-fetoprotein (AFP) level less than or equal to 1000 ng/mL. T2 stage is defined as candidates with *either* of the following:

- One Class 5 lesion greater than or equal to 2 cm and less than or equal to 5 cm in size.
- Two or three Class 5 lesions each greater than or equal to 1 cm and less than or equal to 3 cm in size.

A candidate who has previously had an AFP level greater than 1000 ng/mL at any time must qualify for a standardized MELD or PELD exception according to *Policy 9.5.I.iv: Candidates with Alpha-fetoprotein (AFP) Levels Greater than 1000.*

9.5.I.iii Lesions Eligible for Downstaging Protocols

Candidates are eligible for a standardized MELD or PELD exception if, before completing locoregional therapy, they have lesions that meet *one* of the following criteria:

- One Class 5 lesion greater than 5 cm and less than or equal to 8 cm
- Two or three Class 5 lesions that meet all of the following:
    - At least one lesion greater than 3 cm
    - Each lesion less than or equal to 5 cm, and
    - A total diameter of all lesions less than or equal to 8 cm
- Four or five Class 5 lesions each less than 3 cm, and a total diameter of all lesions less than or equal to 8 cm

For candidates who meet the downstaging criteria above and then complete locoregional therapy, the viable lesions must subsequently meet the size requirements for T2 stage according to *Policy 9.5.I.ii: Eligible Candidates Definition of T2 Stage* to be eligible for a standardized MELD or PELD exception. Downstaging to meet eligibility requirements for T2 stage must be demonstrated by ~~dynamic~~ multiphase contrast-enhanced CT or MRI performed after locoregional therapy. Candidates with lesions that do not initially meet the downstaging protocol inclusion criteria who are later downstaged and then meet eligibility for T2 stage are not automatically eligible for a standardized MELD or PELD exception and must be referred to the NLRB for consideration of a MELD or PELD exception.

9.5.I.iv Candidates with Alpha-fetoprotein (AFP) Levels Greater than 1000

Candidates with lesions meeting T2 stage according to *Policy 9.5.I.ii Eligible Candidates Definition of T2 Stage* but with an alpha-fetoprotein (AFP) level greater than 1000 ng/mL may be treated with locoregional therapy. If the candidate's AFP level falls below 500 ng/mL after treatment, the candidate is eligible for a standardized MELD or PELD exception as long as the candidate's AFP level remains below 500 ng/mL. Candidates with an AFP level greater than or equal to 500 ng/mL following locoregional therapy at any time must be referred to the NLRB for consideration of a MELD or PELD exception.

9.5.I.v Requirements for ~~Dynamic~~ Multiphase Contrast-enhanced CT or MRI of the Liver

CT scans or MRIs performed for a HCC MELD or PELD score exception request must be interpreted by a radiologist at a transplant hospital. If the lesion cannot be categorized due to image degradation or omission, then the lesion will be classified as Not categorizable (NC) and imaging must be repeated or completed to receive an HCC MELD or PELD exception. If the lesion cannot be fully categorized due to image degradation or omission, then imaging must be repeated or completed. Contrast-enhanced ultrasound (CEUS) can be used to determine class 5 classification, in accordance with *Table 9-9*.

9.5.I.vi Imaging Requirements for Class 5 Lesions

Lesions found on imaging in ~~patients~~ candidates at risk for HCC are classified according to *Table 9-9*. The imaging criteria within the table apply only to observations which do not represent benign lesions or non-HCC malignancy (i.e. targetoid or LR-M) by imaging.

Table 9-9: Classification System for Lesions Seen on Imaging of Livers[58]

Seen on Imaging of Livers Class	Description
NC – Not Categorizable	Incomplete or technically inadequate study due to image degradation or omission

5A	Must meet *all* of the following:
	• Maximum diameter of at least 1 cm and less than 2 cm, as measured on late arterial or portal phase images
	• ~~Nonrim arterial phase hyper-enhancement~~
	• Either of the following:
	  • ~~Non-peripheral washout~~
	  • LI-RADS 5 classification on CT, MRI, or CEUS
	  • Biopsy

~~5A-g~~	~~Must meet *all* of the following:~~ • ~~Maximum diameter of at least 1 cm and less than 2 cm, as measured on late arterial or portal phase images~~ • ~~Nonrim arterial phase hyper-enhancement~~ • ~~Threshold growth defined as size increase of a mass by ≥ 50% in ≤ 180 days on MRI or CT~~

[58] LI-RADS criteria is determined by the American College of Radiology. https://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf.

Seen on Imaging of Livers Class	Description

5B	Must meet *all* of the following:
	• Maximum diameter of at least 2 cm and less than or equal to 5 cm, as measured on late arterial or portal phase images
	• ~~Nonrim arterial phase hyper-enhancement~~
	• ~~*One*~~ Either of the following:
	  • ~~Nonperipheral washout~~
	  • ~~Enhancing capsule~~
	  • ~~Threshold growth defined as size increase of a mass by ≥ 50% in ≤ 180 days on MRI or CT~~
	  • LI-RADS 5 classification on CT, MRI, or CEUS
	  • Biopsy

5T	Any Class 5A, ~~5A-g,~~ 5B lesion that was automatically approved upon initial request or extension and has subsequently been treated by locoregional therapy

9.5.I.vii Extensions of HCC Exception

A candidate with an approved exception for HCC is eligible for automatic approval of an extension if the transplant program enters a MELD or PELD Exception Score Extension Request that contains the following:

1. Documentation of the tumor stage using multiphase contrast-enhanced CT or MRI
2. The type of treatment if the number of tumors decreased since the last request
3. The candidate's alpha-fetoprotein (AFP) level

A CT of the chest to rule out metastatic disease is not required after the initial exception request. The candidate's exception extension will then be automatically approved unless *any* of the following occurs:

- The candidate's lesions progress beyond T2 criteria, according to *9.5.I.ii: Eligible Candidates Definition of T2 Stage*
- The candidate's alpha-fetoprotein (AFP) level was less than or equal to 1,000 ng/mL on the initial request but subsequently rises above 1,000 ng/mL
- The candidate's AFP level was greater than 1,000 ng/mL, the AFP level falls below 500 ng/mL after treatment but before the initial request, then the AFP level subsequently rises to greater than or equal to 500 ng/mL
- The candidate's tumors have been resected since the previous request
- The program requests a score different from the scores assigned in Table 9-10.

When a transplant program submits either an initial exception request or the first extension request for a liver candidate at least 18 years old at the time of registration that meets the requirements for a standardized MELD score exception, the candidate will appear on the match run according to the calculated MELD score.

105 A candidate who meets these requirements for a MELD or PELD score exception for HCC will receive a
106 score according to *Table 9-10* below.

107 **Table 9-10: HCC Exception Scores**

Age	Age at registration	Exception Request	Score
At least 18 years old	At least 18 years old	Initial and first extension	Calculated MELD
At least 18 years old	At least 18 years old	Any extension after the first extension	3 points below MMaT
At least 12 years old	Less than 18 years old	Any	40
Less than 12 years old	Less than 12 years old	Any	40

Guidance Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

Guidance to Liver Transplant Programs and the National Liver Review Board for:

Adult MELD Exceptions for Transplant Oncology

Summary and Goals

For many ~~patients~~ candidates with chronic liver disease the risk of death without access to liver transplant can be accurately predicted by the MELD score, which is used to prioritize candidates on the waiting list. However, for some ~~patients~~ candidates the need for liver transplant is not based on the degree of liver dysfunction due to the underlying liver disease but rather a complication of the liver disease. These complications have an increased risk of mortality or waitlist dropout without access to timely transplant and are no reflected in the calculated MELD score.[59] This document summarizes available evidence to assist clinical reviewers in approving candidates for MELD exceptions in the specific setting of hepatic neoplasms. It contains guidance for specific clinical situations for use by the review board to evaluate common exception case requests for adult candidates with the following diagnoses:

- Hepatocellular Carcinoma (HCC)
- Intrahepatic Cholangiocarcinoma (iCCA)
- Neuroendocrine Tumors (NET)
- Colorectal Liver Metastases (CRLM)
- Hepatic Epithelioid Hemangioendothelioma (HEHE)
- Hepatic Adenomas
- ~~Colorectal Liver Metastases (CRLM)~~
- ~~Intrahepatic Cholangiocarcinoma (iCCA)~~

These guidelines are intended to promote consistent review of these diagnoses and summarize the Committee's recommendations to the OPTN Board of Directors.

This resource is not OPTN Policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This resource is intended to provide guidance to transplant programs and the review board.

Background

A liver candidate receives a MELD[60] or, if less than 12 years old, a PELD[61] score that is used for liver allocation. The score is intended to reflect the candidate's disease severity, or the risk of 3-month mortality without access to liver transplant. When the calculated score does not reflect the candidate's medical

[59] Waitlist dropout is removal from the waiting list due to the candidate being too sick to transplant.
[60] Model for End-Stage Liver Disease.
[61] Pediatric End-Stage Liver Disease.

urgency, a liver transplant program may request an exception score. A candidate that meets the criteria for one of nine diagnoses in policy is approved for a standardized MELD exception.[62] If the candidate does not meet criteria for standardized exception, the request is considered by the Review Board.

The OPTN Liver and Intestinal Organ Transplantation Committee (hereafter, "the Committee") has developed guidance for adult MELD exceptions for Transplant Oncology. This guidance document is intended to provide recommendations for the review board considering hepatic neoplasm cases which are outside standard policy.

This guidance replaces any independent criteria that OPTN regions used to request and approve exceptions, commonly referred to as "regional agreements." Review board members and transplant centers should consult this resource when considering MELD exception requests for adult candidates with the following diagnoses.

Instructions for Submitting a Non-Standard exception Request

Instructions for how to submit a non-standard exception request can be found in each relevant diagnosis section. For any other diagnosis that should be reviewed by the Adult Transplant Oncology review board, select "other liver cancer or tumor specify", indicate the diagnosis, and submit a written justification narrative.

Recommendations

Hepatocellular Carcinoma (HCC)

1. ~~Patients with t~~The following are contraindications for HCC exception score:
    - Macro-vascular invasion of main portal vein or hepatic vein
    - Extra-hepatic metastatic disease
    - Ruptured HCC
    - T1 stage HCC

While in most cases, ruptured HCC and primary portal vein branch invasion of HCC would be contraindications, some ~~patients~~ candidates who remain stable for a prolonged (minimum of 12 months) interval after treatment for primary portal vein branch invasion or after ruptured HCC may be suitable for consideration.

Evidence for the use of immunotherapy as a downstaging or bridging therapy is preliminary. However, based on the published data in transplant and non-transplant setting, the use of immunotherapy does not preclude consideration for an HCC exception.[63]

- ~~Patients~~ Candidates beyond standard criteria who have continued progression while waiting despite locoregional are generally not acceptable candidates for HCC MELD exception.
- ~~Patients~~ Candidates with AFP greater than ~~>~~1000 who do not respond to treatment to achieve an AFP below 500 are not eligible for standard MELD exception, and must be reviewed by the Adult Transplant Oncology Review Board to be considered. In general, these ~~patients~~ candidates are not suitable for HCC MELD exception but may be appropriate in some cases.
- ~~Patients~~ Candidates with HCC beyond standard down-staging criteria who are able to be successfully downstaged to T2 may be appropriate for MELD exception, as long as there is no

[62]See OPTN Policy 9.5: Specific Standardized MELD or PELD Exceptions, Available at https://optn.transplant.hrsa.gov/.
[63] Parissa Tabrizian, Sander S. Florman, and Myron E. Schwartz, "PD-1 Inhibitor as Bridge Therapy to Liver Transplantation?," *American Journal of Transplantation* 21, no. 5 (February 2021): pp. 1979-1980, https://doi.org/10.1111/ajt.16448.

evidence of metastasis outside the liver, or macrovascular invasion, or AFP greater than ≥1,000. Imaging should be performed at least 4 weeks after last down-staging treatment. ~~Patients~~ Candidates must still wait for 6 months from the time of the first request to be eligible for an HCC exception score.

- ~~Patients~~ Candidates who presented with stage T2 HCC (LI-RADS 5 or biopsy proven; one lesion greater than ≥2 cm and less than <5 cm in size, two or three lesions greater than ≥1 cm and less than <3 cm in size) which was treated by locoregional therapy or resected but developed T1 or T2 HCC (LI-RADS 5 or biopsy proven) recurrence and the transplant program is requesting an initial HCC exception more than 6 months but less than 60 months following initial treatment or resection are eligible for a MELD score exception without a six month delay period.

~~Patients~~ Candidates with cirrhosis and HCC beyond T2 but within generally accepted criteria for down-staging (such as up to 5 lesions, total tumor volume less than <8 cm based on resection pathology) who underwent complete resection with negative margins and developed T1 or T2 HCC (LI-RADS 5 or biopsy proven) recurrence may also be considered for MELD score exception for HCC. Because the larger tumor size, the 6 month delay is appropriate to ensure favorable tumor biology.

LI-RADS 5 requires the below criteria, which differ based on size and modality. Threshold growth is defined as greater than or equal to 50% increase in longest diameter in less than or equal to 6 months on CT/MRI.[64]

Table 1: LI-RADS 5 Criteria

Imaging Modality[65]	Observation size, mm	LR-5 criteria
CT/MRI	10-19mm	Nonrim arterial phase hyperenhancement (APHE) with at least one of the following: • nonperipheral washout • threshold growth
CT/MRI	Greater than or equal to 20 mm	Nonrim APHE with at least one of the following: • nonperipheral washout • threshold growth • enhancing "capsule"
CEUS	Greater than or equal to 10 mm	Nonrim APHE with: • late and mild washout

[64] American College of Radiology Committee on LI-RADS® (Liver) The LI-RADS v2018 Manual. Available at: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/LIRADS/LI-RADS-2018-Manual-5Dec18.pdf. Accessed on November 6, 2024.

Recommendations for ~~Dynamic~~ Contrast-enhanced ~~m~~Multiphase CT or MRI of the Liver[66]

Table ~~1~~2: Recommendations for ~~Dynamic~~ Contrast-enhanced ~~m~~Multiphase CT of the Liver

Feature:	CT scans should meet the below specifications:
Scanner type	Multidetector row scanner
Detector type	Minimum of 8 detector rows and must be able to image the entire liver during brief late arterial phase time window
Slice thickness	Minimum of 5 mm reconstructed slice thickness; thinner slices are preferable especially if multiplanar reconstructions are performed
Injector	Power injector, preferably dual chamber injector with saline flush and bolus tracking recommended
Contrast injection rate	3 mL/sec minimum, better 4-6 mL/sec with minimum of 300 mg I/mL or higher, for dose of 1.5 mL/kg body weight
Mandatory ~~dynamic~~ multiphase ~~phases~~ on contrast-enhanced MDCT	1. Late arterial phase: ~~artery fully enhanced, beginning contrast enhancement of portal vein~~ hepatic arterial branches are fully enhanced, the hepatic veins are not enhancing, and the portal vein is enhancing more than the liver 2. Portal venous phase: ~~portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins~~ Acquired no more than 120 seconds after injection of a contrast agent when portal and hepatic veins are enhanced more than liver 3. Delayed phase: ~~variable appearance, greater than 120 seconds after initial injection of contrast~~ Acquired at least 120 seconds after injection of contrast when portal and hepatic veins are enhanced more than liver
~~Dynamic~~ Multiphase ~~phases~~ (Timing)	Use the bolus tracking or timing bolus

[66] OPTN Policy 9.5.I requires CT/MRI be Contrast-enhanced Multiphase.

Table ~~23~~: Recommendations for ~~Dynamic~~ Contrast-enhanced Multiphase MRI of the Liver

Feature	MRIs should meet the below specifications:
Scanner type	1.5T Tesla or greater main magnetic field strength. Low field magnets are not suitable.
Coil type	Phased array multichannel torso coil, unless patient-related factors precludes its use.
Minimum sequences	Pre-contrast and ~~dynamic~~ multiphase post gadolinium T1-weighted gradient echo sequence (3D preferable), T2 (with and without fat saturation), T1-weighted in and out of phase imaging.
Injector	Dual chamber power injector with bolus tracking recommended.
Contrast injection rate	2-3 mL/sec of extracellular gadolinium chelate that does not have dominant biliary excretion, preferably resulting in vendor-recommended total dose.
Mandatory ~~dynamic~~ multiphase ~~phases~~ on contrast-enhanced multiphase MRI	1. Pre-contrast T1W: do not change scan parameters for post contrast imaging. 2. Late arterial phase: artery fully enhanced, beginning contrast enhancement of portal vein. 3. Portal venous phase: portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins. 4. Delayed phase: variable appearance, greater than 120 seconds after initial injection of contrast.
~~Dynamic~~ Multiphase ~~phases~~ (Timing)	The use of the bolus tracking method for timing contrast arrival for late arterial phase imaging is preferable. Portal vein phase images should be acquired 35 to 55 seconds after initiation of late arterial phase. Delayed phase images should be acquired 120 to 180 seconds after the initial contrast injection.
Slice thickness	5 mm or less for ~~dynamic~~ multiphase series, 8 mm or less for other imaging.
Breath-holding	Maximum length of series requiring breath-holding should be about 20-seconds with a minimum matrix of 128 x 256. Technologists must understand the importance of patient instruction about breath-holding before and during scan.

Table 4: Recommendations for Contrast-enhanced Ultrasound (CEUS) of the Liver

Feature	CEUSs should meet the below specifications:
Scanner type	Ultrasound scanners equipped with appropriate software and hardware packages for contrast-enhanced imaging
Ultrasound transducer selection	CEUS imaging of the liver is typically performed with a curved array transducer, with higher frequency linear transducers reserved for small superficial liver lesions
Suggested imaging parameters	Dual screen imaging format showing a low mechanical index B-mode image alongside the contrast-only display. An acoustic window that allows the examined lesion to be scanned as close to the transducer as possible maintaining an approximately 2 cm distance from the transducer and allow for the target liver observation to be continuously visible during scanning.
Contrast dose	Contrast dose specified by the manufacturer should be used but the contrast dose may be modified in certain circumstances based on patient factors and sensitivity of the equipment used for CEUS examination
Contrast injection	Intravenous contrast bolus delivered over 2 - 3 seconds immediately followed by a 5–10 mL normal saline flush
Minimum required CEUS images	1. B-mode images of the examined observation 2. Continuous cine loop imaging from first bubble arrival through peak arterial phase enhancement. Optionally, the cine loop can be continued beyond the arterial phase enhancement peak until 60 seconds after injection. 3. Static image at 60 seconds and thereafter, imaging intermittently (every 30-60 seconds) saving static images or short cineloops to document and evaluate the presence, timing, and degree of washout.

To submit an HCC exception request, select *Hepatocellular carcinoma (HCC)* and fill out the associated form. If the candidates does not meet the standardized criteria per *Policy 9.5.I* or seeks a different exception score, the system will direct the transplant program to write and submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board.

Intrahepatic Cholangiocarcinoma

Candidates with biopsy proven unresectable solitary intrahepatic cholangiocarcinoma (iCCA) or mixed hepatocellular carcinoma/intrahepatic cholangiocarcinoma (mixed HCC-iCCA) less than or equal to 3 cm with 6 months of tumor stability after locoregional or systemic therapy should be considered for MELD exception points based on existing data supporting the role of liver transplantation in this setting.[67, 68, 69, 70]

Based on current evidence-based medicine, transplant programs should provide the following elements when submitting an initial MELD exception for iCCA:

- Biopsy proven iCCA or mixed HCC-iCCA[71]
- Presence of cirrhosis
- Unresectable
- Locoregional or systemic therapy for iCCA
- 6 months from time of diagnosis or last treatment of tumor stability meaning less than or equal to 3 cm, no new lesions, or extrahepatic disease before applying for exception

Candidates with iCCA should be considered for a MELD exception extension if they continue to meet *all of* the following criteria:

- Imaging every 3 months to ensure tumor less than or equal to 3 cm
- No extrahepatic disease prior to extending the MELD exception

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3.

To submit an iCCA exception request, select *Cholangiocarcinoma (CCA)* and fill out the associated form. The transplant program will then be directed to submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board. Utilize this same process if submitting an exception request for mixed HCC-iCCA.

Neuroendocrine Tumors (NET)

~~A review of the literature supports that candidates with NET are expected to have a low risk of waiting list drop-out.~~

~~Transplant programs should be aware of the following criteria when submitting exceptions for NET.~~

~~The review board should consider the following criteria when reviewing exception applications for candidates with NET.~~

[67] Sapisochin G, de Lope CR, Gastaca M, de Urbina JO, Lopez-Andujar R, Palacios F, et al. Intrahepatic cholangiocarcinoma or mixed hepatocellular-cholangiocarcinoma in patients undergoing liver transplantation: a Spanish matched cohort multicenter study. Ann Surg; 2014. p. 944-52.

[68] Fu BS, Zhang T, Li H, Yi SH, Wang GS, Xu C. The role of liver transplantation for intrahepatic cholangiocarcinoma: a single-center experience. European Surgical; 2011.

[69] Hayashi A, Misumi K, Shibahara J, Arita J, Sakamoto Y, Hasegawa K, et al. Distinct Clinicopathologic and Genetic Features of 2 Histologic Subtypes of Intrahepatic Cholangiocarcinoma. The American Journal of Surgical Pathology. 2016;40(8):1021-30.

[70] Sapisochin G, Facciuto M, Rubbia-Brandt L, Marti J, Mehta N, Yao FY, et al. Liver transplantation for "very early" intrahepatic cholangiocarcinoma: International retrospective study supporting a prospective assessment. Hepatology. 2016;64(4):1178-88.

[71] There may be worse survival outcomes with poor differentiation of tumor on biopsy.

- ~~Resection of primary malignancy and extra-hepatic disease without any evidence of recurrence for at least six months prior to MELD exception request.~~
- ~~Neuroendocrine Liver Metastasis (NLM) limited to the liver, Bi-lobar, not amenable to resection.~~

~~Tumors in the liver should meet the following radiographic characteristics on *either* CT or MRI:~~

~~1. If CT Scan:~~
   ~~a. Triple phase contrast Lesions may be seen on only one of the three phases~~
   ~~b. Arterial phase: may demonstrate a strong enhancement~~
   ~~c. Large lesions can become necrotic/calcified~~
~~2. If MRI Appearance:~~
   ~~a. Liver metastasis are hypodense on T1 and hypervascular in T2 wave images~~
   ~~b. Diffusion restriction~~
   ~~c. Majority of lesions are hypervascular on arterial phase with wash –out during portal venous phase~~
   ~~d. Hepatobiliary phase post Gadoxetate Disodium (Eovist): Hypointense lesions are characteristics of NET~~

~~1. Consider for exception only those with a NET of Gastro-entero-pancreatic (GEP) origin tumors with portal system drainage. Note: Neuroendocrine tumors with the primary located in the lower rectum, esophagus, lung, adrenal gland and thyroid are not candidates for automatic MELD exception.~~
~~2. Lower - intermediate grade following the WHO classification. Only well differentiated (Low grade, G1) and moderately differentiated (intermediate grade G2). Mitotic rate <20 per 10 HPF with less than 20% ki-67 positive markers.~~
~~3. Tumor metastatic replacement should not exceed 50% of the total liver volume.~~
~~4. Negative metastatic workup should include one of the following:~~
   ~~a. Positron emission tomography (PET scan)~~
   ~~b. Somatostatin receptor scintigraphy~~
   ~~c. Gallium-68 (68Ga) labeled somatostatin analogue 1,4,7,10-tetraazacyclododecane-N, N′, N″,N‴ tetraacetic acid (DOTA)-D-Phe1-Try3- octreotide (DOTATOC), or other scintigraphy to rule out extra-hepatic disease, especially bone metastasis.~~

Candidates with unresectable neuroendocrine liver metastasis limited to the liver, may benefit from liver transplantation. Tumors in the liver should have radiographic or histologic characteristics consistent with neuroendocrine liver metastasis.[72]

1. Only those with a NET of Gastro-entero-pancreatic (GEP) origin tumors with portal system drainage. Neuroendocrine tumors with the primary located in the lower rectum, esophagus, lung, adrenal gland and thyroid are not candidates for MELD exception.
2. Resection of primary malignancy and extra-hepatic disease without any evidence of recurrence at least six months prior to MELD exception request.
3. Lower - intermediate grade following the WHO classification, i.e. well differentiated (low grade, G1) and moderately differentiated (intermediate grade G2), based on primary lesion or the liver metastasis, with mitotic rate less than 20 per 10 HPF and index less than 20%.
4. No evidence for extra-hepatic tumor recurrence based on metastatic radiologic workup at least 3 months prior to initial or extension MELD exception request (submit date). Negative metastatic

[72] Reference: Mazzaferro V, Pulvirenti A, Coppa J. Neuroendocrine tumors metastatic to the liver: how to select patients for liver transplantation? Journal of Hepatology, Oct 2007; 47(4): 460-6.

workup should include functional imaging, e.g. somatostatin receptor scintigraphy, gallium-68 somatostatin receptor imaging, and/or positron emission tomography (PET).

Note: Exploratory laparotomy and or laparoscopy is not required prior to MELD exception request.

Occurrence of extra-hepatic progression – for instance lymph-nodal Ga68 positive locations – should indicate de-listing. Candidates may be re-considered for MELD exception if any extra-hepatic disease is zeroed and remained so for at least 6 months. Presence of extra-hepatic solid organ metastases (i.e. lungs, bones) should be a permanent exclusion.

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT -3.

~~1. No evidence for extra-hepatic tumor recurrence based on metastatic radiologic workup at least 3 months prior to MELD exception request (submit date).~~
~~2. Recheck metastatic workup every 3 months for MELD exception increase consideration by the review board. Occurrence of extra-hepatic progression – for instance lymph-nodal Ga68 positive locations – should indicate de-listing. Patients may come back to the list if any extra-hepatic disease is zeroed and remained so for at least 6 months.~~
~~3. Presence of extra-hepatic solid organ metastases (i.e., lungs, bones) should be a permanent exclusion criteria~~

~~To submit an exception request for NET, select the *Neuroendocrine Tumor (NET)* option. Transplant programs will be directed to write and submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board.~~

Colorectal Liver Metastases

The diagnosis of unresectable colorectal liver metastases (CRLM) has a poor prognosis despite improved local and systemic treatments. Published studies support liver transplantation in highly selected ~~patients~~ candidates and has demonstrated a survival benefit in initial prospective clinical trials.[73, 74, 75, 76]

Based on currently available published studies, transplant programs should provide the following elements when submitting an initial MELD exception for CRLM:

Initial MELD Exception Criteria
Candidates can be considered for MELD exception points for CRLM if all of the following criteria are met:

Primary diagnosis:

- Histological diagnosis of colon/rectal adenocarcinoma
- BRAF wild type, microsatellite stable[77]
- At least 12 months from time of CRLM diagnosis to time of initial exception request

[73] Hagness, M., et al., *Liver transplantation for nonresectable liver metastases from colorectal cancer.* Ann Surg, 2013. 257(5): p. 800-6.
[74] Dueland, S., et al., *Survival Outcomes After Portal Vein Embolization and Liver Resection Compared With Liver Transplant for Patients With Extensive Colorectal Cancer Liver Metastases.* JAMA Surgery, 2021. 156(6): p. 550-557.
[75] Line, P.-D. and S. Dueland, *Liver transplantation for secondary liver tumours: The difficult balance between survival and recurrence.* Journal of Hepatology, 2020. 73(6): p. 1557-1562.
[76] Dueland, S., et al., *Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases.* Annals of Surgery, 2020. 271(2).
[77] Insufficient data to include KRAS as exclusionary factor but should be considered as a negative prognostic factor.

Treatment of primary colorectal cancer

- Standard resection of the primary tumor with negative resection margins
- No evidence of local recurrence by colonoscopy within 12 months prior to time of initial exception request

Evaluation of extrahepatic disease

- No signs of extrahepatic disease or local recurrence, based on CT/MRI (chest, abdomen and pelvis) and PET scan within one month of initial exception request.[78]

Evaluation of hepatic disease and prior systemic/liver directed treatment

- Received or receiving first-line chemotherapy/immunotherapy
- Relapse of liver metastases after liver resection or liver metastases not eligible for curative resection
- No hepatic lesion should be greater than 10 cm before start of treatment
- Must have stability or regression of disease with systemic and/or locoregional therapy for at least 6 months.[79]

In cases of synchronous colon lesions, in addition to above criteria, all of the following are required:

- Resection of the primary tumor is performed more than 6 months after initial diagnosis
- Minimum of 6 months of chemotherapy after primary tumor resection before exception request with stability of disease for a total of at least 12 months after initial diagnosis.[80]

Candidates meeting the criteria described should be considered for a MELD exception score equal to MMaT-20. If MMaT-20 results in an exception score below 15, the candidate's exception score will automatically be set to a MELD score of 15 per OPTN Policy 9.4.E: *MELD or PELD Exception Scores Relative to Median MELD or PELD at Transplant*.

Exclusion Criteria

Candidates should not be considered for an initial MELD exception for CRLM if any of the following criteria are met:

- Extra-hepatic disease after primary tumor resection (including lymphadenopathy outside of the primary lymph node resection)
- Local relapse of primary disease
- Carcinoembryonic antigen (CEA) greater than ~~>~~80 µg/L with or without radiographic evidence of disease progression or new lesion.

MELD Exception Extension Criteria

Candidates with CRLM should be considered for a MELD exception extension if they continue to meet *all of* the following criteria:

- Every 3 months from initial MELD exception:
    - Perform CT or MRI (chest, abdomen and pelvis)
    - Perform CEA testing

[78] Pre transplant PET should be performed after a chemotherapy pause of at least 4 weeks.

[79] Progression is defined as more than 10% increase in diameter of existing lesions (according to RECIST 1.1) OR any new lesions detected on imaging.

[80] Progression is defined as more than 10% increase in diameter of existing lesions (according to RECIST 1.1) OR any new lesions detected on imaging.

- No progression of hepatic disease[81]
- No development of extrahepatic disease
- CEA less than~~<~~ 80 µg/L

To submit an exception request for CRLM, select the *Colorectal liver metastases* option. Transplant programs will be directed to write and submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board.

Hepatic Epithelioid Hemangioendothelioma

Approval of MELD exception points for adult candidates with unresectable Hepatic Epithelioid Hemangioendothelioma (HEHE) may be appropriate in some instances. ~~Biopsy must be performed to establish the diagnosis of HEHE, and exclude hemangiosarcoma.~~ HEHE is a rare, low grade primary liver tumor of mesenchymal cell origin. [82, 83, 84] The presence of extrahepatic disease is not an absolute contraindication. Candidates who are being considered for MELD exception should meet the following criteria.

- Biopsy proven diagnosis of HEHE and exclude hemangiosarcoma.
- Absence of macrovascular invasion on biopsy or imaging.
- Lesions are unresectable.

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3.

~~Because of the rarity of the diagnosis, as well as the variability in presentation, the optimal treatment strategies are not fully established. However, for lesions which cannot be resected, liver transplant is associated with 1, 5, and 10-year patient survival rates of 97%, 83%, and 74%; with more favorable results occurring in patients without microvascular invasion. The presence of extra-hepatic disease has not been associated with decreased survival post liver transplant and therefore should not be an absolute contraindication. Controversy regarding the role of liver transplant in treating HEHE relates to the variable course of disease in the absence of liver transplant, with some patients demonstrating regression or stabilization of disease and prolonged survival.[7]~~

~~To submit an exception request for HEHE, select the *Hepatic Epithelioid Hemangioendothelioma (HEHE)* option. Transplant programs will be directed to write and submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board.~~

Hepatic Adenomas

~~Orthotopic liver transplantation for~~ Liver transplantation for hepatic adenomas (HA) remains a~~n extremely~~ rare ~~indication; however, it is a valid therapeutic option in select patients with adenoma meeting one of the following categories:~~ but viable treatment for select candidates. Candidates may qualify for an exception, if they meet *one* of the following criteria:

[81] Pre transplant PET should be performed after a chemotherapy pause of at least 4 weeks.

[82] Lai Q, et al. HEHE and Adult Liver Transplantation: Proposal for a Prognostic Score Based on the Analysis of the ELTR-ELITA Registry. Transplantation. 2017;101(3):555-564.

[83] Lerut, J.P., G. Orlando, R. Adam, et al. "The place of liver transplantation in the treatment of hepatic epitheloid hemangioendothelioma: report of the European liver transplant registry." Ann Surg 246 (2007): 949-57.

[84] Nudo, C.G., E.M. Yoshida, V.G. Bain, et al. "Liver transplantation for hepatic epithelioid hemangioendothelioma: the Canadian multicentre experience." Can J Gastroenterol 22 (2008):821-4.

- Adenoma in the presence of g~~G~~lycogen s~~S~~torage ~~D~~isease or Abernethy malformation
- Unresectable adenoma with β-c~~C~~atenin ~~(+) Adenoma~~ mutation
- Unresectable adenoma in a ~~patient~~ candidate with liver adenomatosis (great than ~~>~~10 HA)
- Adenoma(s) with all three of the following criteria: ~~below:~~
  - ~~Unresponsive to medical management~~
  - Unresectable
  - Unresponsive to non-operative management (e.g., observation after withholding estrogen-containing medications, observation after efforts to maintain an ideal body weight, transarterial embolization, or radiofrequency ablation)
  - Progressive or with complication such as hemorrhage, rupture, or malignant transformation (~~must specify~~ please provide supportive details including size)

The identification of these criteria is mandatory to aid in the decision-making process.[85,86,87,88]

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3.

To submit an exception request for HA, select the *Hepatic Adenomas* option. Transplant programs will be directed to write and submit a justification narrative that will be reviewed by the Adult Transplant Oncology Review Board.

[85] Blanc, J.F., N. Frulio, L. Chiche, et al. "Hepatocellular adenoma management: call for shared guidelines and multidisciplinary approach." Clinics and research in hepatology and gastroenterology 39 (2015): 180-187.
[86] Chiche, L., A. David, R. Adam, et al. "Liver transplantation for adenomatosis: European experience." Liver Transplantation 22 (2016): 516-526.
[87] Alagusundaramoorthy, S. S., V. Vilchez, A. Zanni, et al. "Role of transplantation in the treatment of benign solid tumors of the liver: a review of the United Network of Organ Sharing data set." JAMA Surgery 150 (2015): 337-342.
[88] Dokmak, S., V. Paradis, V. Vilgrain, et al. "A single-center surgical experience of 122 patients with single and multiple hepatocellular adenomas." Gastroenterology 137 (2009): 1698-1705.

Guidance to Liver Transplant Programs and the National Liver Review Board for:

Adult MELD Exception Review

Summary and Goals

For many ~~patients~~ candidates with chronic liver disease the risk of death without access to liver transplant can be accurately predicted by the MELD score, which is used to prioritize candidates on the waiting list. However, for some ~~patients~~ candidates the need for liver transplant is not based on the degree of liver dysfunction due to the underlying liver disease but rather a complication of the liver disease. These complications have an increased risk of mortality or waitlist dropout without access to timely transplant and are not reflected in the calculated MELD score.[89] This document summarizes available evidence to assist clinical reviewers in approving candidates for MELD exceptions. It contains guidance for specific clinical situations for use by the review board to evaluate common exceptional case requests for adult candidates with the following diagnoses, not all of which are appropriate for MELD exception:

- Ascites
- Budd Chiari
- GI Bleeding
- Hepatic Encephalopathy
- Hepatic Hydrothorax
- Hereditary Hemorrhagic Telangiectasia
- Polycystic Liver Disease (PLD)
- ~~Portopulmonary Hypertension~~
- Primary Sclerosing Cholangitis (PSC) or Secondary Sclerosing Cholangitis (SSC)
- Metabolic Disease
- Multivisceral Transplant Candidates
- Post-Transplant Complications, including Early Allograft Dysfunction (EAD) in Reduced Size Livers (Small for Size Syndrome), Chronic Rejection, Diffuse Ischemic Cholangiopathy~~, and Late Vascular Complications~~
- Pruritus

These guidelines are intended to promote consistent review of these diagnoses and summarize the Committee's recommendations to the OPTN Board of Directors.

This resource is not OPTN Policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This resource is intended to provide guidance to transplant programs and the review board.

[89] Waitlist dropout is removal from the waiting list due to the candidate being too sick to transplant.

Background

A liver candidate receives a MELD[90] or, if less than 12 years old, a PELD[91] score that is used for liver allocation. The score is intended to reflect the candidate's disease severity, or the risk of 3-month mortality without access to liver transplant. When the calculated score does not reflect the candidate's medical urgency, a liver transplant program may request an exception score. A candidate that meets the criteria for one of nine diagnoses in policy is approved for a standardized MELD exception.[92] If the candidate does not meet criteria for standardized exception, the request is considered by the review board.

The OPTN Liver and Intestinal Organ Transplantation Committee (hereafter, "the Committee") has developed guidance for adult MELD exception candidates. The MELD Exceptions and Enhancements Subcommittee proposed these recommendations after reviewing the 2006 MELD Exception Study Group (MESSAGE) Conference, a descriptive analysis of recent MELD exception requests submitted to the OPTN, and available peer-reviewed literature. To support a recommendation for approving additional MELD exception points, there must have been adequate evidence of increased risk of mortality associated with the complication of liver disease.

This guidance replaces any independent criteria that OPTN regions used to request and approve exceptions, commonly referred to as "regional agreements." Review board members and transplant centers should consult this resource when considering MELD exception requests for adult candidates with the following diagnoses.

Recommendation

Ascites

There is inadequate evidence to support granting a MELD exception for ascites in adult candidates with the typical clinical symptoms associated with this diagnosis.

Ascites is a common clinical finding in liver transplant candidates. Refractory ascites, as defined by the International Ascites Club, occurs in 5-10% of patients with portal hypertension and has a 1-year mortality rate of approximately 50%.[93,94,95,96] Hyponatremia is common in patients with cirrhosis and refractory ascites from portal hypertension.[97,98,99] In January 2016, the OPTN implemented a modification to the MELD score to incorporate serum sodium for candidates with a calculated MELD greater than 11.[100] Much of the excess mortality risk related to ascites is similar to portal hypertension and hepatorenal syndrome

[90] Model for End-Stage Liver Disease.
[91] Pediatric End-Stage Liver Disease.
[92] Policy 9.3.C: Specific MELD/PELD Exceptions, Organ Procurement and Transplantation Network Policies.
[93] Moore, K.P., F. Wong, P. Gines, et al. "The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club." Hepatology 38 (2003): 258-66.
[94] Runyon, B.A., AASLD. "Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012." Hepatology 57 (2013): 1651-3.
[95] Runyon, B.A., Committee APG. "Management of adult patients with ascites due to cirrhosis: an update." Hepatology 49 (2009): 2087-107.
[96] Gines P., A. Cardenas, V. Arroyo, et al. "Management of cirrhosis and ascites." N Engl J Med 350 (2004):1646-54.
[97] Biggins, S.W., W.R. Kim, N.A. Terrault, et al. "Evidence-based incorporation of serum sodium concentration into MELD." Gastroenterology 130 (2006):1652-60.
[98] Porcel, A., F. Diaz, P. Rendon, et al. "Dilutional hyponatremia in patients with cirrhosis and ascites." Arch Intern Med 162 (2002):323-8.
[99] Gines, A., A. Escorsell, P. Gines, et al. "Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites." Gastroenterology 105 (1993):229-36.
[100] Biggins, S.W. "Use of serum sodium for liver transplant graft allocation: a decade in the making, now is it ready for primetime?" Liver Transpl 21 (2015):279-81.

and will be accurately reflected in the lab values used to calculate the MELD score, specifically the serum creatinine and serum sodium. Therefore, MELD exception for ascites is not recommended.

Budd Chiari

Approval of MELD exception points for adult candidates with Budd Chiari may be appropriate in some instances.

Liver transplant candidates with Budd Chiari syndrome can be considered for a MELD exception based on severity of liver dysfunction and failure of standard management. Documentation submitted for case review should include all of the following:

- Failed medical or surgical management (please specify)
- Any contraindications to Transjugular Intrahepatic Portosystemic Shunt (TIPS) or TIPS failure; specify specific contraindication
- Documentation that extrahepatic malignancy, which would exclude transplant eligibility, has been ruled out

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3.

Gastrointestinal Bleeding

There is inadequate evidence to support granting a specific MELD exception for gastrointestinal bleeding in adult candidates who experience acute or chronic blood loss independent of their calculated MELD.

There is also inadequate evidence to support a MELD exception for transfusion dependence independent of MELD with one exception, spur cell hemolytic anemia (SCHA).[101] However, due to the infrequent occurrence of SCHA in a transplant candidate, and its common association with recent alcohol use or active infection, MELD exception is not recommended. Similarly there is no evidence to support that candidates with transfusion dependence who develop antibodies while waiting warrant a MELD exception.[102,103]

Hepatic Encephalopathy

Hepatic encephalopathy (HE) is a complication of chronic liver with an associated mortality independent of MELD scoring. Presently, no additional MELD priority for HE is recommended in the absence of a widely

[101]Alexopoulou, A., L. Vasilieva, T. Kanellopoulou, et al. "Presence of spur cells as a highly predictive factor of mortality in patients with cirrhosis." J Gastroenterol Hepatol. 4 (2014):830-4.
[102] Lyles, T., A. Elliott, D.C. Rockey. "A risk scoring system to predict in-hospital mortality in patients with cirrhosis presenting with upper gastrointestinal bleeding." J Clin Gastroenterol 48 (2014):712-20.
[103] Flores-Rendón, A.R., J.A. González-González, D. García-Compean, et al. "Model for end stage of liver disease (MELD) is better than the Child-Pugh score for predicting in-hospital mortality related to esophageal variceal bleeding." Ann Hepatol 7 (2008):230-4.

available, reliable, objective assessment of its severity. [104, 105,106,107]

Hepatic Hydrothorax

~~**There is inadequate evidence to support granting a MELD exception for hepatic hydrothorax in adult candidates with the typical clinical symptoms associated with this diagnosis. Liver transplant candidates with chronic, recurrent, confirmed hepatic hydrothorax could be considered on individual basis for a non-standard MELD exception.**~~

~~Hepatic hydrothorax is a relatively uncommon complication of endstage liver disease occurring in only 5-10% of patients with cirrhosis and portal hypertension.[7] Hepatic hydrothorax can occur in either or both pleural spaces and can occur with or without portal hypertensive ascites. By definition, hepatic hydrothorax is a transudative pleural effusion due to portal hypertension without a cardiopulmonary source. Infectious and malignant pleural effusions must be excluded. In this context, a serum pleural fluid albumin gradient (SPAG) of at least 1.1 g/dL may be more accurate in identifying hepatic hydrothorax than the more traditional Light's criteria for a transudative pleural effusion.[22,] The mostly like explanation for hepatic hydrothorax is passage of fluid from the peritoneal space to the pleural space through diaphragmatic defects which can be documented by intraperitoneal injection of 99MTc-tagged nannocolloids followed by scintigraphy. Unlike ascites, relatively small amounts of fluid in the pleural space (1 to 2 L) lead to severe symptoms such as shortness of breath and hypoxia. Initial management with dietary sodium restriction, diuretics, intravenous albumin, and therapeutic thoracentesis can be successful. Hepatic hydrothorax can be complicated by spontaneous bacterial empyema or iatrogenic complication of thoracentesis (infections, pneumothorax, or hemothorax). For chronic, recurrent, confirmed hepatic hydrothorax, transjugular intrahepatic portosystemic shunt, indwelling pleural catheter, and surgical repair of diaphragmatic defects can be effective in some patients yet risk additional complications. Like ascites, hepatic hydrothorax is similar to portal hypertension and hepatorenal syndrome and will be accurately reflected in the lab values used to calculate the MELD score, specifically the serum creatinine and serum sodium. Therefore, MELD exception for hepatic hydrothorax is not recommended in the majority of circumstances.~~

Candidates with refractory hepatic hydrothorax have an increased mortality that may not otherwise be reflected in the candidate's MELD score and exceeds mortality due to refractory ascites.[108] In addition, the need for inpatient thoracentesis increases risk of acute-on-chronic liver failure (ACLF) compared to candidates with refractory ascites alone.[109] While TIPS can be a viable treatment in some candidates, this

[104] Kerbert, Annarein J., Enric Reverter, Lara Verbruggen, Madelon Tieleman, Miguel Navasa, Bart J. Mertens, Sergio Rodríguez-Tajes, et al. "Impact of Hepatic Encephalopathy on Liver Transplant Waiting List Mortality in Regions with Different Transplantation Rates." *Clinical Transplantation* 32, no. 11 (2018). https://doi.org/10.1111/ctr.13412.

[105] Chiranjeevi Gadiparthi et al., "Waitlist Outcomes in Liver Transplant Candidates with High MELD and Severe Hepatic Encephalopathy," *Digestive Diseases and Sciences* 63, no. 6 (February 2018): pp. 1647-1653, https://doi.org/10.1007/s10620-018-5032-5.

[106] Cristina Lucidi et al., "Hepatic Encephalopathy Expands the Predictivity of Model for End-Stage Liver Disease in Liver Transplant Setting: Evidence by Means of 2 Independent Cohorts," *Liver Transplantation* 22, no. 10 (2016): pp. 1333-1342, https://doi.org/10.1002/lt.24517.

[107] Robert J. Wong, Robert G. Gish, and Aijaz Ahmed, "Hepatic Encephalopathy Is Associated with Significantly Increased Mortality among Patients Awaiting Liver Transplantation," *Liver Transplantation*, 2014, https://doi.org/10.1002/lt.23981.

[108] Higher mortality is associated with HH and mortality rates of 18, 30, and 60% at 6 months, 1 year, and 2 years have been demonstrated (PMID: 36148461). Refractory HH is associated with a higher 1-year mortality than refractory ascites (51% vs 19%, p=0.001) (PMID: PMID: 35534742).

[109] In patients with recurrent ascites, the development of HH was associated with a high mortality-hazard ratio of 4.35 (95% CI: 2.76–6.97)(doi.org/10.1007/s10620-021-07134-8). In addition, HH requiring inpatient thoracentesis associated with increased risk of ACLF (HR = 2.37 vs. refractory ascites alone, p = 0.01, controlling for MELD, AKI, infection, and prior 6-month hospitalizations)

may be contraindicated in others. Therefore, a~~A~~dult liver transplant candidates with chronic, recurrent, ~~confirmed~~ hepatic hydrothorax that are *medically refractory* and for which *TIPS is contraindicated or has failed* [110] could be considered ~~an individual basis~~ for a MELD exception provided that infectious and malignant causes have been ruled out.

Documentation submitted for initial case review should include the following:

- At least ~~1 thoracentesis over~~ 1 L of pleural fluid removed four separate times in 6 weeks ~~weekly in last 4 weeks~~; report date and volume of each ~~thoracentesis~~ pleural fluid removal (including witness attestation by provider or RN if drainage catheter in place).
- Pleural fluid is transudative ~~by pleural albumin-serum albumin gradient of at least 1.1 and by cell count~~ or portal hypertension related by one of the following:
    - Evidence of ascites
    - Pleural albumin-serum albumin gradient greater than or equal to 1.1
- ~~No~~ Echocardiogram without evidence of heart failure~~; provide objective evidence excluding heart failure~~
- Negative pPleural fluid culture or cell count (provide date) ~~negative on 2 separate occasions~~
- Negative pPleural fluid cytology (provide date) ~~is benign on 2 separate occasions~~
- ~~There is contraindications to TIPS; specify specific contraindication~~
- ~~Diuretic refractory~~

Documentation submitted for subsequent maintenance of exception should include the following:

- At least 1 L of pleural fluid removed four separate times in last 6 weeks; report date and volume of each pleural fluid removal (including witness attestation by provider or RN if drainage catheter in place).

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3. Centers will need to update documentation every 90 days to maintain exception status.

Hereditary Hemorrhagic Telangiectasia

Approval of MELD exception points for adult candidates with high output cardiac failure due to multiple arteriovenous (AV) malformations may be appropriate in some instances. Hereditary hemorrhagic telangiectasia is an uncommon, autosomal dominant genetic disorder characterized by mucocutaneous telangiectasias, as well as arteriovenous malformations in the brain, spine, lungs, gastrointestinal tract, and liver. The AV malformations can progress to high output cardiac failure, which eventually may be irreversible[111][112]. ~~In the future, there may be effective non-transplant options, and if such agents become widely available, the recommendation to offer MELD score exception will need to be revisited.~~[7]

(PMID: 33185787). Multivariable modeling also showed that HH increased the risk of inpatient mortality (HR = 2.22 vs. refractory ascites alone, p = 0.04).

[110] Per AASLD guidelines, TIPS placement in patients with MELD scores as low as 18 in some studies and more clearly with MELD score >21 incurs higher mortality risk, and the beneficial outcome in hydrothorax highly relates to liver function and age.

[111] Lee, M., D.Y. Sze, C.A. Bonham, et al. "Hepatic arteriovenous malformations from hereditary hemorrhagic telangiectasia: treatment with liver transplantation." Dig Dis Sci 55 (2010): 3059-62.

[112] Boillot, O., F. Bianco, J.P. Viale, et al. "Liver transplantation resolves the hyperdynamic circulation in hereditary hemorrhagic telangiectasia with hepatic involvement." Gastroenterology 116 (1999): 187-92.

Documentation submitted for case review should include ~~both of~~ the following:

- Documentation of high output cardiac failure by echocardiography or right heart catheterization, and symptoms of heart failure
- Imaging supporting intra-hepatic AV malformations or severe diffuse bilobar hepatic necrosis in the setting of hepatic AV malformation

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT -3. Severe ongoing complications of heart failure may warrant MMaT.

Polycystic Liver Disease (PLD)

~~Patients~~ Candidates with PLD who ~~are not clinically eligible for resection/fenestration or alternative therapy~~ failed medical or surgical management (please specify) may benefit from MELD exception points. Indication for an exception include those with PLD with severe symptoms related to PLD plus *any* of the following:

- Hepatic decompensation or severe portal hypertensive complications
- Concurrent hemodialysis
- GFR less than 20 ml/min
- ~~Patient~~ Candidate with a prior kidney transplant
- Moderate to severe protein calorie malnutrition as documented by a registered dietician using any of the following:
  - Modified Global Leadership Initiative on Malnutrition (GLIM) Phenotypic criteria
  - American Society for Enteral and Parenteral Nutrition (ASPEN) criteria
  - Nutrition Focused Physical Exam (NFPE)
  - Subjective Global Assessment (SGA-C score)
- Severe sarcopenia as documented with skeletal muscle index (SMI less than~~<~~ 39 cm^2/m^2 in women and less than~~<~~ 50 cm^2/m^2 in men)[113] or equivalent

~~Patients~~ Candidates ~~who~~ meeting the criteria described above should be considered ~~are eligible~~ for a MELD exception score equal ~~equivalent~~ to MMaT.

~~Portopulmonary Hypertension~~

~~Candidates meeting the criteria in *Policy 9.5: Specific Standardized MELD or PELD Score Exceptions* are eligible for MELD or PELD score exceptions that do not require evaluation by the full review board.~~

Primary Sclerosing Cholangitis or Secondary Sclerosing Cholangitis

Candidates with Primary Sclerosing Cholangitis (PSC) or Secondary Sclerosing Cholangitis (SSC) may be at risk of adverse outcomes secondary to recurrent sepsis from cholangitis, which may not be reflected in the candidate's calculated MELD score.

Based on clinical experience and a review of the available literature, transplant programs should provide the following elements when submitting exceptions for PSC or SSC and the review board should consider the following elements when reviewing exception applications for candidates with PSC or SSC.

[113] Carey, Elizabeth J., Jennifer C. Lai, Connie W. Wang, Srinivasan Dasarathy, Iryna Lobach, Aldo J. Montano-Loza, and Michael A. Dunn. "A Multicenter Study to Define Sarcopenia in Patients with End-Stage Liver Disease." Liver Transplantation 23, no. 5 (2017): 625–33. https://doi.org/10.1002/lt.24750.

Candidates who meet the following criteria should be considered for a MELD exception equal to MMaT-3:

- The candidate has been admitted to the hospital two or more times within a one-year period with either of the following:
  - Documented blood stream infection
  - Evidence of sepsis with hemodynamic instability requiring vasopressors

In addition, candidates should be considered for a MELD exception score equal to MMaT if they meet at least two of following criteria:

- The candidate has a biliary tract stricture(s) which are not responsive to treatment by interventional radiology (i.e. PTC) or therapeutic endoscopy (ERCP/EUS).
- The candidate has been diagnosed with a high-resistant infectious organism (e.g. Vancomycin Resistant Enterococcus (VRE), Extended Spectrum Beta-Lactamase (ESBL) producing gram-negative organism, Carbapenem-resistant Enterobacteriaceae (CRE) and Multi-drug resistant Acinetobacter).
- The candidate has cirrhosis.

~~The candidate must meet both of the following two criteria:~~

~~1. The candidate has been admitted to the hospital two or more times within a one year period with a documented blood stream infection or evidence of sepsis including hemodynamic instability requiring vasopressors~~
~~2. The candidate has cirrhosis~~

~~In addition the candidate must have one of the following criteria:~~

- ~~The candidate has biliary tract stricture which are not responsive to treatment by interventional radiology (PTC) or therapeutic endoscopy (ERCP) or~~
- ~~The candidate has been diagnosed with a highly resistant infectious organism (e.g. Vancomycin Resistant Enterococcus (VRE), Extended Spectrum Beta-Lactamase (ESBL) producing gram-negative organisms, Carbapenem-resistant Enterobacteriaceae (CRE), and Multidrug-resistant Acinetobacter.)~~

Metabolic Disease

Adults who develop metabolic symptoms secondary to an inherited organic acidemia or urea cycle defect which are typically transplanted during infancy or childhood may be suitable for MELD exception. A ~~Given~~ later onset of metabolic disease may present with mild symptoms and require a MELD exception score equal to MMaT-3. Candidates who present with life-threatening complications of metabolic disease may be considered for a higher exception score.~~, anticipate a reduced urgency compared to early-onset disease, thus priority for transplant may be similar to other exceptions, though if a patient has more urgent medical condition, as reflected by life-threatening complications, a higher priority score can be considered.~~

Multivisceral Transplant Candidates

Multivisceral transplant (MVT) candidates are typically listed for the following organ combinations:

- Liver-intestine-pancreas
- Liver-intestine
- Liver-intestine-pancreas-kidney
- Liver-intestine-kidney

Because MVT candidates require multiple organs from the same donor, these candidates require access to a selective segment of the donor pool. Specifically, for intestine grafts, donors must typically meet the following criteria:

- Donor age less than 40 years old
- Donor should not be on high dose or multiple vasopressors, as this could cause intestine ischemia and dysfunction

For pancreas grafts, donors must typically meet the following criteria:

- Donor body mass index (BMI) should not be high (ideally less than 30)
- Donor should not have pancreatitis or a history of diabetes.

The liver grafts from donors meeting these criteria are often allocated to liver-alone candidates with high MELD or PELD scores before being allocated to MVT candidates. It should be acknowledged that the MELD exception for MVT candidates is not well established. However, candidates listed for a multivisceral transplant should be considered for an initial MELD exception equal to MMaT+6, in order to provide access to suitable donors and avoid waitlist mortality.

Candidates being listed for any liver and kidney multivisceral combination will have already met simultaneous liver-kidney criteria as outlined in OPTN Policy.

Further, MVT candidates should be considered for an additional 3 point increase (e.g. MMaT+9, MMaT+12), every 90 days they remain on the waitlist.

Transplant programs submitting exception requests for MVT candidates should include information on prior exception requests, if applicable. In addition, transplant programs must indicate in the exception narrative the reason the candidate requires a liver and intestine graft with or without a pancreas/kidney. A candidate should not be considered for a MELD exception if the reason he or she requires a liver transplant is solely for immunological reasons.

The following diagnoses are typical indications for multivisceral transplant. This list should be referenced by transplant programs when submitting exceptions for MVT candidates. However, the list should not be considered when determining a candidate's eligibility for a MELD exception. Indications for multivisceral transplant include but are not limited to:

- Intestine failure with liver dysfunction
- Diffuse portomesenteric thrombosis
- Neuroendocrine tumor with liver metastasis
- Unresectable intra-abdominal low-grade malignant tumors involving the liver or hepatic hilum, celiac/SMA trunk
- Catastrophic adhesive disease "Frozen abdomen"

Post-Transplant Complications

Early Allograft Dysfunction (EAD) in Reduced Size Livers (Small for Size Syndrome)

~~Small for size syndrome refers to graft dysfunction of varying severity occurring in the early post-operative period, less than 30 days, following transplantation of a size-reduced liver allograft, with no other identified cause of graft dysfunction such as vascular thrombosis, prolonged ischemia, or other etiology. Typical findings include worsening cholestasis and ascites. With optimal care, some patients may recover~~

~~while others may require re-transplantation.~~

~~**In many cases, the calculated MELD score will provide adequate priority. However, mortality risk may not be adequately reflected by the calculated MELD score in cases of severe dysfunction, and an exception may be appropriate.**~~

Living donor allografts, split allografts, and reduced size allografts are prone to early allograft dysfunction secondary to elevated portal flow or pressure. Symptoms should develop less than 30 days following transplantation without other identified cause of graft dysfunction such as vascular thrombosis, prolonged ischemia, or other etiology. Typical findings include worsening cholestasis, ascites, and renal insufficiency. Key Risk factors include Graft to Recipient Weight Ratio (GRWR) less than 0.8%, Graft Volume to Standard Liver Volume ration of less than 40%, Portal Pressure greater than 15 mm hg or portal cava gradients greater than 10 mm Hg, and Portal flow greater than 250 ml/min/100 gm graft weight.

Documentation submitted for case review should include the anatomy of the split allograft, identified risk factors for small for size syndrome, and any intraoperative or postoperative interventions used for treatment. ~~all of the following:~~

- ~~Risk factor for small for size syndrome~~
- ~~Interventions used to treat small for size syndrome~~
- ~~Clinical status of the patient (hospitalized, requiring ICU care, intubated)~~

With optimal care, many candidates may recover and in many other cases, the calculated MELD score will provide adequate priority. However, candidates with severe allograft dysfunction (Grade C) defined as Total Bilirubin greater than 10 mg/dl and INR greater than 1.6 at day 7 OR Total Bilirubin greater than 20 at day 14 have excess mortality justifying an exception score equal to MMaT.[114]

Chronic Rejection

There is inadequate evidence to support granting a MELD exception for chronic rejection in adult candidates with the typical clinical symptoms associated with this diagnosis.

In cases where re-transplantation is being considered, it is anticipated that progressive injury of the allograft due to rejection will be reflected in the development of liver dysfunction, and prioritization by MELD score may be appropriate. Cases with atypical clinical scenarios in which the degree of liver dysfunction and risk of waitlist mortality are not reflected by the MELD score may be considered on an individual basis.

Diffuse Ischemic Cholangiopathy

Diffuse ischemic cholangiopathy is a complication associated with significant morbidity and may involve multiple biliary interventions and hospitalizations for cholangitis or life-threatening sepsis. It can result from numerous causes including vascular complications, ischemic injury, or receipt of donation after circulatory death (DCD) livers. Due to the highly variable outcomes associated with late hepatic artery thrombosis, there is inadequate evidence to support granting a MELD exception in adult candidates with the typical clinical symptoms, including hepatic abscess and intrahepatic biliary strictures. However, a subset of cases may experience life-threatening infectious complications or persistent long-term morbidity requiring repeat biliary interventions. These candidates may be considered for a MELD exception. ~~donation after circulatory death (DCD) donors. Analysis of waitlist outcomes for patients re-listed after undergoing liver transplant from a DCD donor demonstrates that these patients have a similar or improved~~

[114] A. Kow et al. Transplantation. October 2023; Vol. 107:2226-37.

~~waitlist survival compared to donation after brain death (DBD) candidates who are re-listed with similar MELD scores. However, patients with ischemic cholangiopathy may have significant morbidity and require multiple repeat biliary interventions and repeat hospitalizations for cholangitis. Despite similar waitlist outcomes as DBD donor liver recipients who are listed for retransplant, the Committee supports increased priority for prior DCD donor liver recipients to encourage use of DCD livers when appropriate.~~

~~In addition, analyses has shown that patients with a prior DCD transplant and an approved MELD score exception had an improved survival compared to those who never had an exception approved. Patients with biliary injuries and need for biliary interventions also have been demonstrated to have an increased risk of graft loss and death.~~ **~~Therefore, patients with a prior DCD transplant who demonstrated two or more of the following criteria within 12 months of transplant are eligible for MELD exception equivalent to MMaT:~~**

Documentation for case review should include the following:

1) Risk factor(s) for ischemic cholangiopathy (e.g. hepatic artery thrombosis post-transplant or DCD donor characteristics)
2) Evidence of ischemic cholangiopathy and non-anastomotic biliary stricture, including two or more of the following criteria within 12 months of transplant:
    - Persistent cholestasis as defined by abnormal bilirubin (greater than 2 mg/dl) for greater than 4 weeks
    - Evidence of severe infection, such as:
        - Two or more episodes of cholangitis with an associated bacteremia requiring hospital admission.
        - Repeated multidrug-resistant bacteremia
        - Abscesses and/or biliary strictures requiring frequent interventions (e.g. PTBD, ERCP) requiring at least two documented readmissions over 6 months.
    - ~~Evidence of non-anastomotic biliary strictures not responsive to further treatment~~

Candidates meeting the criteria described above should be considered for a MELD exception score equal to MMaT-3.

~~*Late Vascular Complications*~~

~~Patients with hepatic artery thrombosis occurring within 7 days of transplant with associated severe graft dysfunction may be eligible for Status 1A, or occurring within 14 days of transplantation without severe graft dysfunction may be eligible for a standard exception of 40. Cases of late hepatic artery thrombosis which do not meet these criteria are not eligible for standard MELD exception.~~ **~~Due to the highly variable outcomes associated with late hepatic artery thrombosis, there is inadequate evidence to support granting a MELD exception in adult candidates with the typical clinical symptoms, including hepatic abscess and intrahepatic biliary strictures that may be associated with late HAT. However, patients with atypical severe complications may be considered for MELD exception on an individual basis.~~**
~~Complications that warrant consideration of MELD exception are similar to those criteria noted for DCD cholangiopathy (with 2 or more episodes of cholangitis requiring hospital admission over a 3 months period plus biliary strictures not responsive to further treatment or bacteremia with highly resistant organisms). Patients with early HAT just beyond 7 or 14 day cut off with evidence of severe graft dysfunction may be considered for MELD exception, depending on the clinical scenario.~~

Pruritus

There is inadequate evidence to support granting a MELD exception for pruritus in adult candidates with the typical clinical symptoms associated with this diagnosis. Pruritus is a manifestation of predominantly cholestatic liver diseases. It had been reported that chronic pruritus may lead to a decreased quality of life, prolonged wound healing, skin infections, and sleep disturbance.[115] The frequency ranges from 80-100% for patients suffering from Primary Biliary Cirrhosis; 20-40% for patients with primary Sclerosing Cholangitis and Chronic Viral Hepatitis among other diseases.[116] The pruritus increases as the disease is progresses. So far data have failed to support an endpoint related to quantity but rather of quality of life and were considered inappropriate for additional MELD points.[117] Due to inadequate evidence of increased risk of pre-transplant mortality, or a widely-accepted threshold for access to liver transplant, MELD score exception for isolated clinical finding of pruritus is not recommended.

Conclusion

Review board members should consult this resource when assessing adult MELD exception requests. Liver programs should also consider this guidance when submitting exception requests for adult candidates with these diagnoses. However, these guidelines are not prescriptive of clinical practice.

[115] Pruritus in chronic cholestatic liver disease. Bunchorntavakul C, Reddy KR Clin Liver Dis. 2012 May;16(2):331-46.
[116] Elman, S., L.S. Hynan, V. Gabriel, et al. "The 5-D itch scale: a new measure of pruritus." Br J Dermatol 162 (2010): 587-93.
[117] Martin, P., A. DiMartini, S. Feng, et al. "Evaluation for liver transplantation in adults: 2013 practice guideline by the AASLD and the American Society of Transplantation." (2013): 61.

National Liver Review Board Operational Guidelines

Overview

The purpose of the National Liver Review Board (NLRB) is to provide fair, equitable, and prompt peer review of exceptional candidates whose medical urgency is not accurately reflected by the calculated MELD/PELD score. The NLRB will base decisions on policy, the guidance documents, and in cases which lack specific guidance, the medical urgency of the candidate as compared to other candidates with the same MELD or PELD score adjustment or specific MELD or PELD score.

The NLRB is comprised of specialty boards, including:

- Adult Transplant Oncology
- Adult Other Diagnosis
- Pediatrics, which reviews requests made on behalf of any candidate registered prior to turning 18 years old ~~and adults with certain pediatric diagnoses~~

The immediate past-Chair of the Liver and Intestinal Organ Transplantation Committee serves as the Chair of the NLRB for a two year term.

Representation

Every active liver transplant program may appoint a representative and alternate to each of the adult specialty boards. A liver transplant program with an active pediatric component may appoint a representative and alternate to the pediatric specialty board. Individuals may serve on more than one specialty board at the same time. Transplant programs are encouraged to appoint representatives from both hepatology and surgery who have active transplant experience. Liver transplant programs are not required to provide a representative to the NLRB.

Representatives and alternates serve a one year term. A liver transplant program may appoint the same representative or alternate to serve consecutive terms.

If a transplant hospital withdraws or inactivates its liver program, it may not participate in the NLRB. However, the transplant hospital's participation may resume once it has reactivated its liver program.

Representative and Alternate Responsibilities

Prior to each term of service, representatives and alternates are required to sign the *OPTN Confidentiality and Conflict of Interest Statement* and complete orientation training.

Representatives must vote within 7 days on all exception requests, exception extension requests, and appeals. A representative will receive an e-mail reminder after day 3 and day 5 if the representative has an outstanding vote that must be completed. On the eighth day, if the vote has not been completed, then the request will be randomly reassigned to another representative. The original reviewer will receive a notification that the request has been reassigned.

The representative must notify the OPTN in the OPTN Computer System of an absence, during which the alternate will fulfill the responsibilities of the representative

If a representative or alternate does not vote on an open request within 7 days on more than 5% of the cases assigned to that reviewer within a 6 month period, the Chair may remove the individual from the NLRB. If a representative or alternate does not vote because a case is approved and closed before the 7 day timeframe expires, it is not considered a failure to vote. A representative or alternate who has been removed for failure to perform the duties required is not eligible to serve again for 3 years.

If a transplant program exhibits a pattern of non-responsiveness, as evidenced by the removal of two members from the NLRB, the Chair may suspend the program's participation for a period of three months after notifying the program director. Further non-compliance with the review board process may result in cessation of the program's representation on the NLRB until such a time as the transplant hospital can satisfactorily assure the Chair that it has addressed the causes of non-compliance.

Voting Procedure

An exception request is randomly assigned to five representatives of the appropriate specialty board. A representative may vote to approve or deny the request, or ask that the request be reassigned. The request must achieve four out of five affirmative votes in order to be approved. If the request does not achieve the necessary four affirmative votes, it is denied.

As part of the MELD/PELD Exception program in the OPTN Computer System NLRB members are notified of new cases by email.

Voting on an exception request is closed either at the end of the appeal period or when no additional votes will change the outcome of the vote, whichever occurs earlier. Members no longer have the ability to vote once a request is closed.

Appeal Process

A liver program may appeal the NLRB's decision to deny an exception request. ~~Patients~~ Candidates are not eligible to appeal exception requests. All reviewer comments are available in the OPTN Computer System. The NLRB advises programs to respond to the comments of dissenting reviewers in the appeal.

The same five members that reviewed the original request will review the appeal. The appeal must achieve four out of five affirmative votes in order to be approved. If the appeal does not achieve the necessary four affirmative votes, it is denied. If the appeal is denied, the liver program may request a conference call with the Appeals Review Team (ART).

If the ART denies the request, the liver program may initiate a final appeal to the Liver and Intestinal Organ Transplantation Committee (Liver Committee). Referral of cases to the Liver Committee will include information about the number of previous referrals from that program and the outcome of those referrals.

Appeals Review Team (ART)

At the beginning of each new service term, nine NLRB members from the Adult Other Diagnosis and Adult Transplant Oncology specialty boards are assigned to serve each month of the year on the Adult ART and nine NLRB members from the Pediatric specialty board are assigned to serve each month of the year on the Pediatric ART. There may be multiple ARTs, depending on the volume of cases. Each ART will be scheduled to meet via conference call according to a predetermined schedule.

ART appeals from the Adult Other Diagnosis and Adult Transplant Oncology specialty boards will be reviewed by the Adult ART. ART appeals from the Pediatric specialty board will be reviewed by the Pediatric ART.

In the event of a planned absence, the ART member may designate their alternate to serve. The representative must notify the OPTN of this in the OPTN Computer System.

Five members of the ART must participate in the call. If at least five members do not attend the call, the appeal will be rescheduled for the following regularly scheduled conference call. If at least five members do not attend the second attempt to review the appeal, the candidate's exception request is automatically approved.

The appeal must achieve a majority plus one affirmative votes in order to be approved.

A representative at the petitioning program may serve as the candidate's advocate. If a representative is unable to attend the conference call, the program may ask for the appeal to be scheduled for the following regularly scheduled conference call. If after two attempts a representative is unable to attend the call, the ART will review the appeal without the program's participation. In the absence of a representative on the conference call, the program may submit written information for the ART's consideration.

A current member of the Liver Committee serving on either the Adult Other Diagnosis specialty board or Adult Transplant Oncology specialty board will be appointed to serve as the ART leader for the Adult ART prior to each service term. A current member of the Liver Committee or current member of the OPTN Pediatric Transplantation Committee (Pediatric Committee) serving on the Pediatric specialty board will be appointed to serve as the ART leader for the Pediatric ART prior to each service term. If no current member of either the Liver Committee or the Pediatric Committee is available to serve as the ART leader, prior members of each Committee or other members of the NLRB may be appointed to serve as ART leader. The ART leader will be prepared to lead ART discussion and provide feedback to the Liver Committee.

The ART will work with the OPTN to document the content of the discussion and final decision in OPTN Computer System.

Liver Committee Review

The Liver Committee may delegate review to a subcommittee. If the review is delegated, majority is based on the size of the subcommittee.

Appeals to the Liver Committee will be considered electronically unless at least one member of the Liver Committee requests a conference call. If the case is discussed on a conference call, quorum is a majority of the Liver Committee (or the subcommittee, if delegated).

The appeal must achieve a majority affirmative votes in order to be approved.

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