OPTN

Notice of OPTN Guidance Changes

Continued Review of National Liver Review Board (NLRB) Guidance

Sponsoring Committee:	**OPTN Liver and Intestinal Organ Transplantation**
Guidance Affected:	***Guidance to Liver Transplant Programs and the National Liver Review Board for Adult MELD Exception Review*** ***Guidance to Liver Transplant Programs and the National Liver Review Board for Pediatric MELD/PELD Exception Review***
Public Comment:	**August 3, 2022 - September 28, 2022**
Board Approved:	**December 5, 2022**
Effective Date:	**January 5, 2023**

Purpose of Guidance Changes

The purpose of the NLRB, which was implemented on May 14, 2019, is to provide equitable access to transplant for liver 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. The purpose of this proposal is to make improvements to the NLRB guidance documents, including creating guidance for pediatric liver transplant candidates with cystic fibrosis and updating guidance for adult liver transplant candidates with hepatic adenomas and Budd-Chiari syndrome.

Proposal History

Prior to the implementation of the NLRB, MELD and PELD exception requests were reviewed by regional review boards (RRBs). The implementation of the NLRB was a significant change in the process for reviewing MELD or PELD exception requests and because of the significance and complexity of the change, the Committee has continued to receive feedback on areas for improvement to the NLRB guidance. This proposal represents the Committee's commitment to continue to improve the NLRB.

[1] *Proposal to Establish a National Liver Review Board,* OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, Available at https://optn.transplant.hrsa.gov/.

Summary of Changes

The proposal includes the following changes:

- Pediatric Cystic Fibrosis Guidance: The proposal adds guidance for pediatric transplant candidates with cystic fibrosis. The guidance provides a pathway to a MELD or PELD exception for pediatric liver-alone transplant candidates meeting the following criteria:
    - Candidates who have portal hypertension with complications and have failed or are not candidates for medical, endoscopic or surgical interventions to prevent or treat these complications.
    - Candidates who have growth failure as a result of their liver disease, defined by age and sex-specific weight, length/height, weight-for-length, and/or body mass index (BMI) percentiles or have moderate to severe malnutrition.[2]
    - Candidates who have a forced expiratory volume at 1 second (FEV_1) less than 70% or evidence of decline in FEV_1 of greater than or equal to 5% per year.[3]
- Hepatic Adenomas Guidance: The proposal updates the guidance for adult transplant candidates with hepatic adenomas by removing an unnecessary introductory paragraph, updating the criteria to better capture population of candidates needing a MELD exception, and removing references to "multiple" hepatic adenomas.
- Budd-Chiari Syndrome Guidance: The proposal updates the guidance for candidates with Budd-Chiari Syndrome by removing an unnecessary introductory paragraph, adding failed surgical management as a qualifying criterion, removing the requirement for programs to provide etiology of hypercoagulable state, and removing the criterion related to decompensated hepatic hydrothorax requiring thoracentesis, which is already covered in guidance for hepatic hydrothorax.

Implementation

Liver transplant programs and NLRB reviewers will need to be familiar with the changes when submitting and reviewing MELD or PELD exception requests.

The OPTN will update the guidance documents on the OPTN website and provide communications to the liver transplant community.

Affected Guidance Language

New language is underlined (<u>example</u>) and language that is deleted is struck through (~~example~~).

Guidance to Liver Transplant Programs and the National Liver Review Board for: Pediatric MELD/PELD Exception Review

<u>Cystic Fibrosis</u>

<u>The current criteria for a standard exception for cystic fibrosis (CF) outlined in *OPTN Policy 9.5: Specific Standardized MELD or PELD Score Exceptions* often do not apply to children and adolescents with CF-</u>

[2] Katherine Cheng et al., "Liver Transplant in Children and Adults with Cystic Fibrosis: Impact of Growth Failure and Nutritional Status," *American Journal of Transplantation* 22, no. 1 (September 2, 2021): pp. 177-186, https://doi.org/10.1111/ajt.16791.
[3] A. Jay Freeman et al., "A Multidisciplinary Approach to Pretransplant and Posttransplant Management of Cystic Fibrosis–Associated Liver Disease," *Liver Transplantation* 25, no. 4 (2019): pp. 640-657, https://doi.org/10.1002/lt.25421.

related liver disease (CFLD) who are listed for liver-only transplant. The major causes of liver-related morbidity and mortality in children with CFLD include cirrhosis with hepatic dysfunction and microscopic portal venopathy, leading to portal hypertension without hepatic dysfunction. CF-related comorbidities, including lung disease, sinusitis, CF-related diabetes, multi-drug resistant organisms and pancreatic insufficiency, may impact survival as well.

Calculated MELD or PELD scores may underestimate the risk of waitlist mortality for pediatric liver candidates with CFLD, particularly in those with complications of portal hypertension or with other CF-related morbidities. **Evidence currently supports that pediatric liver transplant candidates with CFLD should be considered for additional MELD or PELD exception points when any of the following criteria are met:**

- Candidate has portal hypertension with complications and the transplant program demonstrates that the patient has failed or is not a candidate for medical, endoscopic or surgical interventions to prevent or treat these complications.
- Candidate has growth failure as a result of liver disease, defined by age and sex-specific weight, length/height, weight-for-length, and/or BMI percentiles or has moderate to severe malnutrition. Children and adolescents with CF and growth failure have a higher risk of waitlist mortality than children with non-CF related liver disease and therefore calculated MELD or PELD may not fully capture their risk of mortality.[4]
- Candidate has an FEV_1 <70% or evidence of decline in FEV_1 of ≥5% per year, as these children may be expected to move toward advanced lung disease, reducing the opportunity for liver transplant.[5]

Since CFLD is an uncommon indication for liver transplant, there is minimal direct evidence on mortality risk conferred by other CF-related morbidities in CF liver transplant candidates. Other CF-related morbidities should thus be considered as justification for MELD or PELD exceptions on a case-by-case basis.

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

~~Multiple~~ Hepatic Adenoma~~s~~

~~Hepatic adenomas (HA) are rare benign nodules occurring principally in women taking oral contraceptives, are solitary or multiple, and highly variable in size; there is no consensus for their management except that once their size exceeds 5 cm nodules are resected to prevent 2 major complications: bleeding and malignant transformation. An exception to this is in men where it is recommended to remove smaller nodules. The presence of HCC in HA is a well-documented observation, the risk ranging from 5 to 9%; gene coding for β-catenin mutations (15-18% of cases) are~~

[4] Katherine Cheng et al., "Liver Transplant in Children and Adults with Cystic Fibrosis: Impact of Growth Failure and Nutritional Status," *American Journal of Transplantation* 22, no. 1 (September 2, 2021): pp. 177-186, https://doi.org/10.1111/ajt.16791.
[5] A. Jay Freeman et al., "A Multidisciplinary Approach to Pretransplant and Posttransplant Management of Cystic Fibrosis–Associated Liver Disease," *Liver Transplantation* 25, no. 4 (2019): pp. 640-657, https://doi.org/10.1002/lt.25421.

~~associated with a high risk of malignant transformation (together with cytologic atypia). HA are a frequent mode of presentation in some genetic diseases, particularly Glycogen Storage Disease (GSD) and congenital or acquired vascular anomalies.~~

Orthotopic liver transplantation for hepatic adenoma (HA) remains an extremely rare indication; however, it is a valid therapeutic option in select patients with adenoma meeting one of the following categories: ~~with risk of malignant transformation, not amenable to resection (the reason must be provided), and one or more of the following~~:

- ~~Malignant transformation proven by biopsy~~
- ~~Presence of glycogen storage disease which increases the risk for malignant transformation~~
- 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)

The identification of these criteria is mandatory to aid in the decision-making process.

Budd-Chiari

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

~~Budd-Chiari syndrome is an uncommon manifestation of hepatic vein thrombosis and patients might present with evidence of decompensated portal hypertension (ascites and hepatic hydrothorax) among others. Medical management may include diuresis and anticoagulation; or more aggressive management with Transjugular Intrahepatic Portosystemic Shunt (TIPS), portosystemic shunting, or liver transplant. Anticoagulation and pharmacologic management is the cornerstone treatment. Patients with severe portal hypertension not controlled with the standard of care might have evidence of hyponatremia or renal impairment, but these will be accurately reflected by the calculated MELD score.~~

Liver transplant candidates with Budd-Chiari syndrome ~~could~~ can be considered ~~on an individual basis~~ 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)
- ~~Etiology of hypercoagulable state~~
- Any contraindications to Transjugular Intrahepatic Portosystemic Shunt (TIPS) or TIPS failure; specify specific contraindication
- ~~Decompensated portal hypertension in the form of hepatic hydrothorax requiring thoracentesis more than 1 liter per week for at least 4 weeks (transudate, no evidence of empyema, and negative cytology or any evidence of infection).~~
- Documentation that extrahepatic malignancy has been ruled out