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# MEDICAL POLICY – 7.03.509

# Liver Transplant and Combined Liver-Kidney Transplant

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| BCBSA Ref. Policy: | 7.03.06 |
| Effective Date: | Dec. 1, 2025 |
| Last Revised: | Nov. 11, 2025 |
| Replaces: | N/A |

RELATED MEDICAL POLICIES:

| | |
|---|---|
| 7.03.01 | Kidney Transplant |
| 8.01.11 | Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies |

**Select a hyperlink below to be directed to that section.**

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | APPENDIX | HISTORY

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## Introduction

An organ transplant is the surgical process of replacing a severely diseased organ with a healthy one from a donor. The donated organ can come from a living person or a person who passed away from an accident or illness. Organ failure is the most common reason a transplant is needed. Organ failure can occur because of illness, injury, or birth defect. There are many factors that go into finding a donor organ that matches. These include blood type and the size of the organ. Other factors include how long a person has been on the waiting list, the level of illness, and the distance the donated organ must be transported. This policy describes when transplanting a liver or a liver/kidney combined may be considered medically necessary. This policy notes that a plan physician will review solid organ transplant requests together with the criteria of the transplant center.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

| Transplant | Medical Necessity |
|---|---|
| **Liver transplant using a cadaver or living donor** | **A liver transplant using a cadaver or living donor may be considered medically necessary for carefully selected individuals with end-stage liver failure due to irreversibly damaged livers. Etiologies of end-stage liver disease include, but are not limited to, the following:**<br>A. Hepatocellular diseases<br>o Alcoholic liver disease<br>o Viral hepatitis (either A, B, C, or non-A, non-B)<br>o Autoimmune hepatitis<br>o α1-Antitrypsin deficiency<br>o Hemochromatosis<br>o Metabolic dysfunction-associated steatohepatitis (MASH)<br>o Protoporphyria<br>o Wilson disease<br>B. Cholestatic liver diseases<br>o Primary biliary cirrhosis<br>o Primary sclerosing cholangitis with development of secondary biliary cirrhosis<br>o Biliary atresia<br>C. Vascular disease<br>o Budd-Chiari syndrome<br>D. Primary hepatocellular carcinoma (see **Related Information** for individual selection criteria)<br>E. Inborn errors of metabolism<br>F. Trauma and toxic reactions<br>G. Miscellaneous<br>o Familial amyloid polyneuropathy |
| **Liver transplantation** | **Liver transplantation may be considered medically necessary in individuals with polycystic disease of the liver who have massive hepatomegaly causing obstruction or functional impairment.**<br>**Liver transplantation may be considered medically necessary in individuals with unresectable hilar (extrahepatic)** |

| Transplant | Medical Necessity |
|---|---|
| | **cholangiocarcinoma (see Related Information for individual selection criteria).**<br><br>**Liver transplantation may be considered medically necessary in pediatric individuals with nonmetastatic hepatoblastoma.**<br><br>**Liver transplantation is considered not medically necessary in the following individuals:**<br>• Individuals with hepatocellular carcinoma that has extended beyond the liver (see **Related Information** for individual selection criteria)<br>• Individuals with ongoing alcohol and/or drug abuse **except** for those with:<br>  ○ Objective failure of therapy for severe acute alcoholic hepatitis.[73] (See **Appendix** for Lille protocol), **or**<br>  ○ Critical decompensation in alcohol related cirrhotic individuals as judged by Model for End-stage Liver Disease score (MELD-Na ≥21)[68] predicting mortality prior to completion of required abstinence<br><br>**Note**: Evidence for abstinence may vary among liver transplant programs, but generally a minimum of 3 months is required. |
| **Liver retransplantation** | **Liver retransplantation may be considered medically necessary in individuals with:**<br>• Primary graft nonfunction<br>• Hepatic artery thrombosis<br>• Chronic rejection<br>• Ischemic type biliary lesions after donation after cardiac death<br>• Recurrent non-neoplastic disease-causing late graft failure |
| **Combined liver-kidney transplantation** | **Combined liver-kidney transplantation may be considered medically necessary in individuals who qualify for liver transplantation and have advanced irreversible kidney disease.** |

| Transplant | Investigational |
|---|---|
| **Liver transplantation** | **Liver transplantation is considered investigational in the following situations:** |

| Transplant | Investigational |
|---|---|
| | • Individuals with neuroendocrine tumors metastatic to the liver<br>• Individuals with intrahepatic cholangiocarcinoma<br>• Individuals with hepatic adenoma<br>• Individuals with unresectable colorectal liver metastases<br>• Individuals with epithelioid hemangioendothelioma (HEHE)<br><br>**Liver transplantation is considered investigational in all other situations not described above.** |

| Documentation Requirements |
|---|
| **The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:**<br>• Office visit notes that contain the relevant history and physical supporting that the individual has end stage liver disease due to an irreversibly damaged liver from one of the listed etiologies. Request for liver transplant, combined liver/kidney transplant, or liver retransplantation is specified. |

**Note**: Combined liver-kidney transplant would be reported with the codes in this policy along with the codes in the policy on kidney transplant (See **Related Policies**).

## Coding

| Code | Description |
|---|---|
| **CPT** | |
| 47135 | Liver allotransplantation; orthotopic; partial or whole, from cadaver or living donor, any age |
| **HCPCS** | |
| S2152 | Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and posttransplant care in the global definition |

**Note**: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

# Related Information

## Contraindications

Potential contraindications for solid organ transplant are subject to the judgment of the transplant center and include the following:

- Known current malignancy, including metastatic cancer
- Recent malignancy with high risk of recurrence
- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage diseases not attributed to liver disease
- History of cancer with a moderate risk of recurrence
- Systemic disease that could be exacerbated by immunosuppression
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy.

## Liver-Specific Criteria

The Model for End-stage Liver Disease (MELD) and Pediatric End-stage Liver Disease (PELD) scores range from 6 (less ill) to 40 (gravely ill). The MELD and PELD scores will change during an individual's tenure on the waiting list.

Individuals with liver disease related to alcohol or drug abuse must be actively involved in a substance abuse treatment program.

Tobacco consumption is a contraindication.

Individuals with polycystic disease of the liver do not develop liver failure but may require transplantation due to the anatomic complications of a hugely enlarged liver. The MELD and PELD score may not apply to these cases. One of the following complications should be present:

- Enlargement of liver impinging on respiratory function
- Extremely painful enlargement of liver
- Enlargement of liver significantly compressing and interfering with function of other abdominal organs.

Individuals with familial amyloid polyneuropathy do not experience liver disease per se but develop polyneuropathy and cardiac amyloidosis due to the production of a variant transthyretin molecule by the liver. MELD and PELD exception criteria and scores may apply to these cases. Candidacy for liver transplant is an individual consideration based on the morbidity of the polyneuropathy. Many Individuals may not be candidates for liver transplant alone due to coexisting cardiac disease.

## Hepatocellular Carcinoma

Criteria used for selection of hepatocellular carcinoma (HCC) individuals eligible for liver transplant include the Milan criteria, which is considered the criterion standard, the University of California, San Francisco expanded criteria, and United Network of Organ Sharing (UNOS) criteria.

## Milan Criteria

A single tumor 5 cm or less or 2 to 3 tumors 3 cm or less.

## University of California, San Francisco Expanded Criteria

A single tumor 6.5 cm or less or up to 3 tumors 4.5 cm or less, and a total tumor size of 8 cm or less.

## UNOS Stage T2 Criteria

A single tumor 2 cm or greater and up to 5 cm or less or two to three tumors 1 cm or greater and up to 3 cm or less and without extrahepatic spread or macrovascular invasion. UNOS criteria were updated in 2022.

Individuals with HCC are appropriate candidates for liver transplant only if the disease remains confined to the liver. Therefore, the individual should be periodically monitored while on the waiting list, and if metastatic disease develops, the individual should be removed from the transplant waiting list. Also, at the time of transplant, a backup candidate should be scheduled. If locally extensive or metastatic cancer is discovered at the time of exploration before hepatectomy, the transplant should be aborted, and the backup candidate scheduled for transplant.

Note that liver transplantation for those with T3 HCC is not prohibited by UNOS guidelines, but such individuals do not receive any priority on the waiting list. All individuals with HCC awaiting transplantation are reassessed at three-month intervals. Those whose tumors have progressed and are no longer stage T2, will lose the additional allocation points.

Additionally, nodules identified through imaging of cirrhotic livers are given a class 5 designation. Class 5B and 5T nodules are eligible for automatic priority. Class 5B criteria consists of a single nodule 2 cm or larger and up to 5 cm (T2 stage) that meets specified imaging criteria. Class 5T nodules have undergone subsequent locoregional treatment after being automatically approved on initial application or extension. A single class 5A nodule (>1 cm and <2 cm) corresponds to T1 HCC and does not qualify for automatic priority. However, combinations of class 5A nodules are eligible for automatic priority if they meet stage T2 criteria. Class 5X lesions are outside of stage T2 and ineligible for automatic exception points. Nodules less than 1 cm are considered indeterminate and are not considered for additional priority. Therefore, the UNOS allocation system provides strong incentives to use locoregional therapies to downsize tumors to T2 status and to prevent progression while on the waiting list.

## Cholangiocarcinoma

According to the Organ Procurement and Transplantation Network (OPTN) policy on liver allocation, candidates with cholangiocarcinoma meeting the following criteria will be eligible for a MELD or PELD exception with a 10% mortality equivalent increase every three months:

- Centers must submit a written protocol for individual care to the OPTN and UNOS Liver and Intestinal Organ Transplantation Committee before requesting a MELD score exception for a candidate with cholangiocarcinoma. This protocol should include selection criteria, administration of neoadjuvant therapy before transplantation, and operative staging to exclude individuals with regional hepatic lymph node metastases, intrahepatic metastases, and/or extrahepatic disease. The protocol should include data collection as deemed necessary by the OPTN and UNOS Liver and Intestinal Organ Transplantation Committee.

- Candidates must satisfy diagnostic criteria for hilar cholangiocarcinoma: malignant-appearing stricture on cholangiography and one of the following: carbohydrate antigen 19-9 100 U/mL, or biopsy or cytology results demonstrating malignancy, or aneuploidy. The tumor should be considered unresectable on the basis of technical considerations or underlying liver disease (e.g., primary sclerosing cholangitis).
- If cross-sectional imaging studies (computed tomography scan, ultrasound, magnetic resonance imaging) demonstrate a mass, the mass should be less than 3 cm.
- Intra- and extrahepatic metastases should be excluded by cross-sectional imaging studies of the chest and abdomen at the time of initial exception and every three months before score increases.
- Regional hepatic lymph node involvement and peritoneal metastases should be assessed by operative staging after completion of neoadjuvant therapy and before liver transplantation. Endoscopic ultrasound-guided aspiration of regional hepatic lymph nodes may be advisable to exclude individuals with obvious metastases before neoadjuvant therapy is initiated.
- Transperitoneal aspiration or biopsy of the primary tumor (either by endoscopic ultrasound, operative, or percutaneous approaches) should be avoided because of the high risk of tumor seeding associated with these procedures.

## Living Donor Criteria

Donor morbidity and mortality are prime concerns in donors undergoing right lobe, left lobe, or left lateral segment donor partial hepatectomy as part of living donor liver transplantation. Partial hepatectomy is a technically demanding surgery, the success of which may be related to the availability of an experienced surgical team. The American Society of Transplant Surgeons proposed the following guidelines for living donors (American Society of Transplant Surgeons: Ethics Committee. American Society of Transplant Surgeons' position paper on adult-to-adult living donor liver transplantation. Liver Transplant. 2000;6(6):815-817. PMID 11084076):

- They should be healthy individuals who are carefully evaluated and approved by a multidisciplinary team including hepatologists and surgeons to assure that they can tolerate the procedure
- They should undergo evaluation to ensure that they fully understand the procedure and associated risks

- They should be of legal age and have sufficient intellectual ability to understand the procedures and give informed consent
- They should be emotionally related to the recipients
- They must be excluded if the donor is felt or known to be coerced
- They need to have the ability and willingness to comply with long-term follow-up.

## Benefit Application

See individual's plan contract language for organ transplant benefits and specific benefits related to transport, lodging, and donor services. Please note limitations in coverage based on the transplant benefit, if applicable.

# Evidence Review

## Description

Liver transplantation is currently the treatment of last resort for individuals with end-stage liver disease. Liver transplantation may be performed with a liver donation after a brain or cardiac death or with a liver segment donation from a living donor. Individuals are prioritized for transplant by mortality risk and severity of illness criteria developed by the Organ Procurement and Transplantation Network (OPTN) and the United Network of Organ Sharing (UNOS). The severity of illness is determined by the Model for End-stage Liver Disease (MELD) and Pediatric End-stage Liver Disease (PELD) scores.

## Background

Solid organ transplantation offers a treatment option for individuals with different types of end stage organ failure that can be lifesaving or provide significant improvements to an individual's quality of life.[1] Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation.

Transplant recipients require life-long immunosuppression to prevent rejection. Individuals are prioritized for transplant by mortality risk and severity of illness criteria developed by OPTN and UNOS.

## Liver Transplantation

Liver transplantation is routinely performed as a treatment of last resort for individuals with end-stage liver disease. Liver transplantation may be performed with liver donation after a brain or cardiac death or with a liver segment donation from a living donor. Certain populations are prioritized as Status 1A (e.g., acute liver failure with a life expectancy of fewer than 7 days without a liver transplant) or Status 1B (pediatric individuals with chronic liver disease). Following Status 1, donor livers are prioritized to those with the highest scores on the MELD and PELD scales. Due to the scarcity of donor livers, a variety of strategies have been developed to expand the donor pool. For example, a split graft refers to dividing a donor liver into two segments that can be used for two recipients. Living donor liver transplantation (LDLT) is now commonly performed for adults and children from a related or unrelated donor. Depending on the graft size needed for the recipient, either the right lobe, left lobe, or the left lateral segment can be used for LDLT. In addition to addressing the problem of donor organ scarcity, LDLT allows the procedure to be scheduled electively before the recipient's condition deteriorates or serious complications develop. LDLT also shortens the preservation time for the donor liver and decreases disease transmission from donor to recipient.

## Summary of Evidence

For individuals who have a hepatocellular disease who receive a liver transplant, the evidence includes registry studies and systematic reviews. The relevant outcomes include overall survival (OS), morbid events, and treatment-related morbidity and mortality. Studies on liver transplantation for viral hepatitis have found that survival is lower than for other liver diseases. Although these statistics raise questions about the most appropriate use of a scarce resource (donor livers), the long-term survival rates are significant in a group of individuals who have no other treatment options. Also, survival can be improved by the eradication of the hepatitis virus before transplantation. For individuals with metabolic dysfunction-associated steatohepatitis (MASH), OS rates have been shown to be similar to other indications for liver transplantation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have primary HCC who receive a liver transplant, the evidence includes systematic reviews of observational studies. The relevant outcomes include OS, morbid events,

and treatment-related morbidity and mortality. In the past, long-term outcomes in individuals with primary hepatocellular malignancies had been poor (19%) compared with the OS of liver transplant recipients. However, the recent use of standardized individual selection criteria (e.g., the Milan criteria diameter) has dramatically improved OS rates. In the appropriately selected individuals, a liver transplant has been shown to result in higher survival rates than resection. In individuals who present with unresectable organ-confined disease, transplant represents the only curative approach. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have extrahepatic cholangiocarcinoma who receive a liver transplant, the evidence includes systematic reviews of observational studiesand individual registry studies. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. For individuals with extrahepatic (hilar or perihilar) cholangiocarcinoma who are treated with adjuvant chemotherapy, 5-year survival rates have been reported as high as 76%. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have intrahepatic cholangiocarcinoma who receive a liver transplant, the evidence includes registry studies and a systematic review of observational studies. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. In a registry study comparing outcomes in individuals with intrahepatic cholangiocarcinoma who received liver transplantation to those who received surgical resection of the liver, no differences were found in OS, length of stay, or unplanned 30-day readmission rates between groups. Additional studies reporting survival rates in individuals with intrahepatic cholangiocarcinoma or in mixed populations of individuals with extrahepatic and intrahepatic cholangiocarcinoma have reported 5-year survival rates of less than 30%. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have metastatic neuroendocrine tumors (NETs) who receive a liver transplant, the evidence includes systematic reviews of case series. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. In select individuals with nonresectable, hormonally active liver metastases refractory to medical therapy, liver transplantation has been considered as an option to extend survival and minimize endocrine symptoms. While some centers may perform liver transplants on select individuals with neuroendocrine tumors, the available studies are limited by their heterogeneous populations. Further studies are needed to determine the appropriate selection criteria. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable colorectal liver metastases who receive a liver transplant, the evidence includes one randomized controlled trial (RCT) and nonrandomized studies. Relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. Five-year OS was improved with liver transplant compared with standard of care in the RCT. Nonrandomized studies indicate improved OS compared with historic controls. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable hepatic epithelioid hemangioendothelioma (HEHE) who receive a liver transplant, the evidence includes nonrandomized, observational studies. Relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. Posttransplant survival among individuals with HEHE was similar to those undergoing liver transplant for other indications. Based on the lack of standard treatment and the rare tumor type, high-quality comparative trials are unlikely to be conducted for hepatic transplant in HEHE. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have hepatic adenomas who receive a liver transplant, the evidence includes nonrandomized observational studies and a systematic review of these studies. Relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. The systematic review found 5-year OS rates of 95% but noted a lack of optimal selection criteria for individuals with hepatic adenoma who would benefit from hepatic transplant. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have pediatric hepatoblastoma who receive a liver transplant, the evidence includes case series. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. The literature on liver transplantation for pediatric hepatoblastoma is limited, but case series have demonstrated good outcomes and high rates of long-term survival. Additionally, nonmetastatic pediatric hepatoblastoma is among the UNOS criteria for individuals eligible for liver transplantation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a failed liver transplant who receive a liver retransplant, the evidence includes observational studies. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. Case series have demonstrated favorable outcomes with liver retransplantation in certain populations, such as when criteria for original liver transplantation are met for retransplantation. While some evidence has suggested outcomes after retransplantation may be less favorable than for initial transplantation in some individuals,

long-term survival benefits have been demonstrated. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with indications for liver and kidney transplant who receive a combined liver-kidney transplant (CLKT), the evidence includes a systematic review of retrospective observational studies in adults and several individual registry studies. The relevant outcomes include OS, morbid events, and treatment-related morbidity and mortality. Most of the evidence involves adults with cirrhosis and kidney failure. Indications for CLKT in children are rare and often congenital and include liver-based metabolic abnormalities affecting the kidney, along with structural diseases affecting both the liver and kidney. In both adults and children, comparisons with either liver or kidney transplantation alone would suggest that CLKT is no worse, and possibly better, for graft and individual survival. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

## Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in **Table 1**.

## Table 1. Summary of Key Trials

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| **Ongoing** | | | |
| NCT05717842 | Simultaneous Prospective Kidney Transplant Assessment in Combined Liver Kidney | 15 | Feb 2026 |

NCT: national clinical trial

## Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

## 2012 Input

In response to requests, input was received from three physician specialty societies and five academic medical centers while this policy was under review in 2012. There was a consensus among reviewers that liver transplantation may be medically necessary for end-stage liver failure due to irreversibly damaged livers from various disease states such as those considered during the report update. There was also a consensus among reviewers that liver retransplantation is appropriate in individuals with acute or chronic liver failure such as primary graft nonfunction, ischemic-type biliary injury after donation after cardiac death, hepatic artery thrombosis, chronic rejection or recurrent diseases such as primary sclerosing cholangitis, autoimmune hepatitis, and hepatitis C resulting in end-stage liver failure. There was general support for the use of liver transplantation as a treatment for cholangiocarcinoma in individuals who meet strict eligibility criteria. In general, there was no support for the use of liver transplantation for a neuroendocrine tumor metastatic to the liver.

## Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a United States (US) professional society, an international society with US representation, or National Institute for Health and Care Excellence. Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

## International Consensus Conference

In 2010, an International Consensus Conference, including representation from the US, convened with the goal of reviewing current practice regarding liver transplantation in individuals with HCC.[79] The Conference ultimately came up with recommendations beginning from the assessment of candidates with HCC for liver transplantation and managing individuals on waitlists, to the role of liver transplantation and post-transplant management. Some notable recommendations are described.

The Milan criteria were recommended for use as the benchmark for individual selection, although it was suggested that the Milan criteria might be modestly expanded based on data from expansion studies that demonstrated outcomes are comparable with outcomes from studies using the Milan criteria. Candidates for liver transplantation should also have a predicted survival of five years or more. The consensus criteria indicate alpha-fetoprotein concentrations may be used with imaging to assist in determining individual prognosis.

Regarding liver retransplantation, the consensus criteria issued a weak recommendation for retransplantation after graft failure of a living donor transplant for HCC in individuals meeting regional criteria for a deceased donor liver transplant. A strong recommendation was issued against liver retransplantation with a deceased donor for graft failure for individuals exceeding regional criteria. Also, the consensus criteria issued a strong recommendation that liver retransplantation for recurrent HCC would not be appropriate. However, a de novo case of HCC may be treated as a new tumor, and retransplantation may be considered even though data to support this is limited.

In 2024, another international joint conference was held, convening the International Liver Transplantation Society (ILTS) and International Liver Cancer Association (ILCA) to update its consensus on liver transplantation for HCC and intrahepatic cholangiocarcinoma.[80,] Similarly to 2010, the Conference came up with recommendations beginning from the assessment of candidates with HCC or intrahepatic cholangiocarcinoma and managing individuals on waitlists, to the role of liver transplantation and post-transplantation management. Some notable recommendations are summarized in Table 2, below.

## Table 2. Notable Recommendations From 2024 ILTS and ILCA Conference on Liver Transplantation in HCC and iCCA

| Recommendation | Quality of evidence | Grade of recommendation |
|---|---|---|
| **HCC** | | |
| Liver transplantation should not be restricted to HCC individuals who have a predicted 5-year survival rate comparable to non-HCC individuals. However, organ availability in different regions should be considered in allocation policies to avoid disadvantaging non-HCC individuals. | Moderate | Moderate |

| | | |
|---|---|---|
| Criteria for listing individuals with HCC for liver transplantation must not rely solely on tumor size and number and should consider biomarkers (mainly AFP) and their dynamics on the waitlist. Emerging data suggest the use of AFP-L3, DCP, and PET-CT can add prognostic value. | Moderate | Strong |
| Salvage liver transplantation in indivduals with HCC recurrence or liver insufficiency can be as safe and effective as primary transplantation for HCC in individuals that meet transplantation criteria. | Weak | Moderate |
| Given that the outcomes with regards to overall and disease-free survival are on-par and, in certain cases, better than DDLT, LDLT should be considered as an oncologically durable and safe alternative to DDLT. In regions where the waiting time (>3 mo) or where LDLT is the predominant type of LT, LDLT may be a preferred option for HCC within and beyond standard criteria. | Moderate | Moderate |
| **iCCA** | | |
| In cirrhotic individuals with iCCA, liver transplantation may be considered as a potential therapeutic option in tumors ≤3 cm in diameter after a period of observation with stability and without extrahepatic metastasis, as it offers a chance of curative treatment and improved survival. | Moderate | Moderate |
| In non-cirrhotic individuals with intrahepatic cholangiocarcinoma, liver transplantation is not routinely recommended but may be considered as part of investigational protocols for individuals with unresectable, liver-confined disease after at least 6 mo of stability after systemic therapy. Limitations on tumor size and number should be explored in prospective clinical trials. | Moderate | Weak |

AFP: alpha-fetoprotein; DCP: des-gamma-carboxy prothrombin; DDLT: deceased donor liver transplantation; HCC: hepatocellular carcinoma; iCCA: intrahepatic cholangiocarcinoma; ILCA: International Liver Cancer Association; ILTS: International Liver Transplantation Society; LDLT: living donor liver transplantation; LT: liver transplantation; PET-CT: positron emission tomography-computed tomography

Many recommendations deferred to local or regional protocols, but there seemed to be interest in expansion of liver transplantation protocols from the 2010 consensus.

## American Association for the Study of Liver Diseases and American Society of Transplantation

In 2013, the American Association for the Study of Liver Diseases (AASLD) and the American Society of Transplantation (AST) issued joint guidelines on evaluating individuals for a liver transplant.[74] These guidelines indicated liver transplantation for severe acute or advanced chronic liver disease after all effective medical treatments have been attempted. The formal evaluation should confirm the irreversible nature of the liver disease and lack of effective alternative medical therapy.

The guidelines also stated that liver transplant is indicated for the following conditions:

- Acute liver failure complications of cirrhosis
- Liver-based metabolic conditions with systemic manifestations
    - α1-Antitrypsin deficiency
    - Familial amyloidosis
    - Glycogen storage disease
    - Hemochromatosis
    - Primary oxaluria
    - Wilson disease
- Systemic complications of chronic liver disease.

The guidelines also included 1-A recommendations (strong recommendation with high-quality evidence) for a liver transplant that:

- "Tobacco consumption should be prohibited in LT [liver transplant] candidates."
- "Individuals with HIV [Human Immunodeficiency Virus] infection are candidates for LT if immune function is adequate and the virus is expected to be undetectable by the time of LT."
- "LT candidates with HCV [hepatitis C virus] have the same indications for LT as for other etiologies of cirrhosis."

Contraindications to liver transplant included:

- "MELD [Model for End-stage Liver Disease] score < 15
- Severe cardiac or pulmonary disease
- AIDS [acquired immunodeficiency syndrome]
- Ongoing alcohol or illicit substance abuse
- Hepatocellular carcinoma with metastatic spread
- Uncontrolled sepsis
- Anatomic abnormality that precludes liver transplantation
- Intrahepatic cholangiocarcinoma
- Extrahepatic malignancy
- Fulminant hepatic failure
- Hemangiosarcoma
- Persistent noncompliance
- Lack of adequate social support system."

In 2014, the AASLD, AST, and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition issued joint guidelines on the evaluation of the pediatric individuals for liver transplant.[75] The guidelines stated that "disease categories suitable for referral to a pediatric LT program are similar to adults: acute liver failure, autoimmune, cholestasis, metabolic or genetic, oncologic, vascular, and infectious. However, specific etiologies and outcomes differ widely from adult patients, justifying independent pediatric guidelines." The indications listed for liver transplantation included biliary atresia, Alagille syndrome, pediatric acute liver failure, hepatic tumors, HCC, hemangioendothelioma, cystic fibrosis-associated liver disease, urea cycle disorders, immune-mediated liver disease, along with other metabolic or genetic disorders.

## The American Association for the Study of Liver Diseases

In 2019, the AASLD guideline on alcohol-associated liver disease provided recommendations on the timing of referral and selection of candidates for liver transplant.[76] The guidance notes that the individual's history of addiction to alcohol is a primary driver in selecting appropriate candidates for liver transplantation. Clinical characteristics that should trigger an evaluation and

consideration for liver transplant include decompensated alcohol-associated cirrhosis, Child-Pugh-Turcotte class C cirrhosis, or a MELD-Na score ≥21. Additionally, the guideline notes that candidate selection "should not be based solely on a fixed interval of abstinence" and instead a formal psychological evaluation can help stratify individuals into higher- or lesser-risk strata for relapse.

In 2023, the AASLD released a practice guideline on the management of HCC.[77] Evidence recommendations by the expert panel are rated based on the Oxford Center for Evidence-Based Medicine and the strength of recommendations are categorized based on the level of evidence, risk–benefit ratio, and individual preferences. Recommendations regarding liver transplantation are listed below.

- "Liver transplantation should be the treatment of choice for transplant-eligible patients with early-stage HCC occurring in the setting of clinically significant portal hypertension and/or decompensated cirrhosis (Level 2, Strong Recommendation)
- AASLD advises the use of pre-transplant locoregional bridging therapy for patients being evaluated or listed for liver transplantation, if they have adequate hepatic reserve, to reduce the risk of waitlist dropout in the context of anticipated prolonged wait times for transplant (Level 3, Strong Recommendation)
- AASLD advises individuals with decompensated cirrhosis who develop T1 HCC and are eligible for LT be monitored with cross-sectional imaging at least every 3 months until criteria are met for MELD exception before pursuing LRT [locoregional therapy] (Level 3, Weak Recommendation)
- Individuals who are otherwise transplant-eligible except with initial tumor burden exceeding the Milan criteria, especially those meeting United Network of Organ Sharing (UNOS) downstaging criteria, should be considered for LT following successful downstaging to within Milan criteria after a 3-to-6-month period of observation (Level 2, Strong Recommendation)
- AASLD advises surveillance for detection of post-transplant HCC recurrence using multiphasic contrast-enhanced abdominal CT [computed tomography] or MRI [magnetic resonance imaging] and chest CT scan (Level 2, Strong Recommendation)"

In July 2025, AASLD published a critical update to the guidance based on newly published data.[78,] However, the update was related to immunotherapy in the adjuvant setting and did not change any previous recommendations related to transplantation.

## National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guidelines on HCC (v 1.2025) recommend referral to a liver transplant center or bridge therapy for individuals with HCC meeting United Network of Organ Sharing (UNOS) criteria of a single tumor measuring 2 to 5 cm, or two to three tumors 1 to 3 cm in diameter with no macrovascular involvement or extrahepatic disease.[16] In individuals who are ineligible for transplant and in select individuals with Child-Pugh class A or B liver function with tumors that are resectable, and who fit UNOS criteria/ extended criteria, the NCCN indicates that these individuals could be considered for resection or transplant. Individuals with unresectable HCC should be evaluated for liver transplantation; if the individual is a transplant candidate, then referral to a transplant center should be given or bridge therapy should be considered. The NCCN guidelines also indicate that individuals with unresectable disease who are not a transplant candidate should receive locoregional therapy with ablation, arterially directed therapies, or external beam radiation therapy or may receive systemic therapy, best supportive care, or be enrolled in a clinical trial. These are level 2A recommendations based on lower-level evidence and uniform consensus.

The NCCN guidelines on neuroendocrine tumors (v.2.2025) indicate that liver transplantation for neuroendocrine liver metastases is considered investigational despite "encouraging" 5-year survival rates.[81]

## National Liver Review Board

In July 2025, the board revised guidance for specific clinical situations to evaluate common exception case requests for adult liver transplant candidates.[82] 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. This guidance replaces any independent criteria that OPTN regions used to request and approve exceptions, commonly referred to as “regional agreements.” This guidance document is intended to provide recommendations for the review board considering hepatic neoplasm cases which are outside standard policy.

They should use this resource when considering MELD 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

## Hepatocellular Carcinoma

Individuals with the following are contraindications for HCC exception score:

- Macro-vascular invasion of main portal vein or hepatic vein
- Extrahepatic metastatic disease
- Ruptured HCC
- T1 stage HCC

## Intrahepatic Cholangiocarcinoma

According to the OPTN policy on liver allocation, candidates with unresectable intrahepatic cholangiocarcinoma can be considered if all of the following criteria are met:

- Biopsy-proven, unresectable, solitary intrahepatic cholangiocarcinoma or mixed hepatocellular carcinoma/intrahepatic cholangiocarcinoma;
- History of locoregional or systemic therapy;
- ≤3 cm tumor with stable disease for 6 months (no new lesions or extrahepatic disease) and imaging every 3 months to ensure tumor is ≤3 cm.

## Neuroendocrine Tumors

According to the OPTN policy on liver allocation, candidates with unresectable neuroendocrine liver metastasis can be considered if all of the following criteria are met:

- Tumor must be of gastro-entero-pancreatic (GEP) origin 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);
- Resection of primary malignancy and extrahepatic disease without any evidence of recurrence for ≥6 months;
- Lower-intermediate grade following the WHO classification;
- No evidence for extrahepatic tumor recurrence based on metastatic radiologic workup ≥3 months prior to initial or extension MELD exception request (negative metastatic workup should include functional imaging).

## Colorectal Liver Metastases

According to the OPTN policy on liver allocation, candidates with unresectable colorectal liver metastases can be considered if all of the following criteria are met:

- Primary diagnosis of colon/rectal adenocarcinoma that is BRAF wild type and microsatellite stable of at least 12 months duration;
- Standard resection of the primary tumor with negative resection margins and no evidence of local recurrence by colonoscopy within 12 months prior to request;
- No signs of extrahepatic disease or local recurrence;
- Received or receiving first-line chemo- or immunotherapy with stability or disease regression with systemic and/or locoregional therapy for at least 6 months;
- Individuals with synchronous colon lesions must also have resection of the primary tumor more than 6 months after initial diagnosis and a minimum of 6 months of chemotherapy after primary tumor resection with disease stability of at least 12 months after diagnosis.

## Hepatic Epithelioid Hemangioendothelioma

According to the OPTN policy on liver allocation, candidates with unresectable hepatic epithelioid hemangioendothelioma (HEHE) can be considered if all of the following criteria are met:

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

## Hepatic Adenoma

According to the OPTN policy on liver allocation, candidates with unresectable hepatic adenoma can be considered if one of the following criteria are met:

- Adenoma in the presence of glycogen storage disease or Abernethy malformation;
- Unresectable adenoma with β-catenin mutation;
- Unresectable adenoma in a candidate with liver adenomatosis (greater than 10 HA);
- Adenoma(s) with all 3 of the following criteria:
    - 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 complications such as hemorrhage, rupture, or malignant transformation.

## Medicare National Coverage

Medicare covers adult liver transplantation for end-stage liver disease and HCC when performed in a facility approved by the Centers for Medicare & Medicaid Services (CMS) as meeting institutional coverage criteria for liver transplants. [83,84] The following conditions must be met for coverage of HCC:

- "The individual is not a candidate for subtotal liver resection;
- The individual's tumor(s) is less than or equal to 5 cm in diameter;
- There is no macrovascular involvement; and

- There is no identifiable extrahepatic spread of tumor to surrounding lymph nodes, lungs, abdominal organs or bone; and
- The transplant is furnished in a facility that is approved by CMS [Centers for Medicare & Medicaid Services] ..."

Beginning in June 2012, on review of this national coverage decision for new evidence, Medicare began covering adult liver transplantation, at Medicare administrative contractor discretion, for extrahepatic unresectable cholangiocarcinoma, liver metastases due to a neuroendocrine tumor, and hemangioendothelioma. Adult liver transplantation is excluded from other malignancies.

Pediatric liver transplantation is covered for children (<18 years of age) when performed at pediatric hospitals approved by the CMS. Coverage includes extrahepatic biliary atresia or any other form of end-stage liver disease, except for children with a malignancy extending beyond the margins of the liver or those with persistent viremia.

## Regulatory Status

Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the US Food and Drug Administration (FDA).

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Solid organs used for transplantation are subject to these regulations.

## References


1. Black CK, Termanini KM, Aguirre O, et al. Solid organ transplantation in the 21 st century. Ann Transl Med. Oct 2018; 6(20): 409. PMID 30498736
2. Belle SH, Beringer KC, Detre KM. An update on liver transplantation in the United States: recipient characteristics and outcome. Clin Transpl. 1995: 19-33. PMID 8794252
3. Sheiner P, Rochon C. Recurrent hepatitis C after liver transplantation. Mt Sinai J Med. 2012; 79(2): 190-8. PMID 22499490
4. Gadiparthi C, Cholankeril G, Perumpail BJ, et al. Use of direct-acting antiviral agents in hepatitis C virus-infected liver transplant candidates. World J Gastroenterol. Jan 21 2018; 24(3): 315-322. PMID 29391754
5. Wang X, Li J, Riaz DR, et al. Outcomes of liver transplantation for nonalcoholic steatohepatitis: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. Mar 2014; 12(3): 394-402.e1. PMID 24076414

6. Yong JN, Lim WH, Ng CH, et al. Outcomes of Nonalcoholic Steatohepatitis After Liver Transplantation: An Updated Meta-Analysis and Systematic Review. Clin Gastroenterol Hepatol. Jan 2023; 21(1): 45-54.e6. PMID 34801743

7. Cholankeril G, Wong RJ, Hu M, et al. Liver Transplantation for Nonalcoholic Steatohepatitis in the US: Temporal Trends and Outcomes. Dig Dis Sci. Oct 2017; 62(10): 2915-2922. PMID 28744836

8. Schoenberg MB, Bucher JN, Vater A, et al. Resection or Transplant in Early Hepatocellular Carcinoma. Dtsch Arztebl Int. Aug 07 2017; 114(31-32): 519-526. PMID 28835324

9. Zheng Z, Liang W, Milgrom DP, et al. Liver transplantation versus liver resection in the treatment of hepatocellular carcinoma: a meta-analysis of observational studies. Transplantation. Jan 27 2014; 97(2): 227-34. PMID 24142034

10. Guiteau JJ, Cotton RT, Washburn WK, et al. An early regional experience with expansion of Milan Criteria for liver transplant recipients. Am J Transplant. Sep 2010; 10(9): 2092-8. PMID 20883543

11. Pomfret EA, Washburn K, Wald C, et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. Liver Transpl. Mar 2010; 16(3): 262-78. PMID 20209641

12. Ioannou GN, Perkins JD, Carithers RL. Liver transplantation for hepatocellular carcinoma: impact of the MELD allocation system and predictors of survival. Gastroenterology. May 2008; 134(5): 1342-51. PMID 18471511

13. Chan EY, Larson AM, Fix OK, et al. Identifying risk for recurrent hepatocellular carcinoma after liver transplantation: implications for surveillance studies and new adjuvant therapies. Liver Transpl. Jul 2008; 14(7): 956-65. PMID 18581511

14. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. Mar 14 1996; 334(11): 693-9. PMID 8594428

15. Firl DJ, Kimura S, McVey J, et al. Reframing the approach to patients with hepatocellular carcinoma: Longitudinal assessment with hazard associated with liver transplantation for HCC (HALTHCC) improves ablate and wait strategy. Hepatology. Oct 2018; 68(4): 1448-1458. PMID 29604231

16. National Comprehensive Cancer Network. Hepatocellular Carcinoma. Version 1.2025. **https://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf**. Accessed October 13, 2025.

17. Yadav DK, Chen W, Bai X, et al. Salvage Liver Transplant versus Primary Liver Transplant for Patients with Hepatocellular Carcinoma. Ann Transplant. Aug 03 2018; 23: 524-545. PMID 30072683

18. Murali AR, Patil S, Phillips KT, et al. Locoregional Therapy With Curative Intent Versus Primary Liver Transplant for Hepatocellular Carcinoma: Systematic Review and Meta-Analysis. Transplantation. Aug 2017; 101(8): e249-e257. PMID 28282359

19. Maggs JR, Suddle AR, Aluvihare V, et al. Systematic review: the role of liver transplantation in the management of hepatocellular carcinoma. Aliment Pharmacol Ther. May 2012; 35(10): 1113-34. PMID 22432733

20. Chan DL, Alzahrani NA, Morris DL, et al. Systematic review of efficacy and outcomes of salvage liver transplantation after primary hepatic resection for hepatocellular carcinoma. J Gastroenterol Hepatol. Jan 2014; 29(1): 31-41. PMID 24117517

21. Zhu Y, Dong J, Wang WL, et al. Short- and long-term outcomes after salvage liver transplantation versus primary liver transplantation for hepatocellular carcinoma: a meta-analysis. Transplant Proc. Nov 2013; 45(9): 3329-42. PMID 24182812

22. Cambridge WA, Fairfield C, Powell JJ, et al. Meta-analysis and Meta-regression of Survival After Liver Transplantation for Unresectable Perihilar Cholangiocarcinoma. Ann Surg. Feb 01 2021; 273(2): 240-250. PMID 32097164

23. Gu J, Bai J, Shi X, et al. Efficacy and safety of liver transplantation in patients with cholangiocarcinoma: a systematic review and meta-analysis. Int J Cancer. May 01 2012; 130(9): 2155-63. PMID 21387295

24. Heimbach JK. Successful liver transplantation for hilar cholangiocarcinoma. Curr Opin Gastroenterol. May 2008; 24(3): 384-8. PMID 18408469

25. Darwish Murad S, Kim WR, Harnois DM, et al. Efficacy of neoadjuvant chemoradiation, followed by liver transplantation, for perihilar cholangiocarcinoma at 12 US centers. Gastroenterology. Jul 2012; 143(1): 88-98.e3; quiz e14. PMID 22504095

26. Heimbach JK, Gores GJ, Haddock MG, et al. Predictors of disease recurrence following neoadjuvant chemoradiotherapy and liver transplantation for unresectable perihilar cholangiocarcinoma. Transplantation. Dec 27 2006; 82(12): 1703-7. PMID 17198263

27. Rea DJ, Heimbach JK, Rosen CB, et al. Liver transplantation with neoadjuvant chemoradiation is more effective than resection for hilar cholangiocarcinoma. Ann Surg. Sep 2005; 242(3): 451-8; discussion 458-61. PMID 16135931

28. Pascher A, Jonas S, Neuhaus P. Intrahepatic cholangiocarcinoma: indication for transplantation. J Hepatobiliary Pancreat Surg. 2003; 10(4): 282-7. PMID 14598146

29. Friman S, Foss A, Isoniemi H, et al. Liver transplantation for cholangiocarcinoma: selection is essential for acceptable results. Scand J Gastroenterol. Mar 2011; 46(3): 370-5. PMID 21073376

30. Meyer CG, Penn I, James L. Liver transplantation for cholangiocarcinoma: results in 207 patients. Transplantation. Apr 27 2000; 69(8): 1633-7. PMID 10836374

31. Robles R, Figueras J, Turrión VS, et al. Spanish experience in liver transplantation for hilar and peripheral cholangiocarcinoma. Ann Surg. Feb 2004; 239(2): 265-71. PMID 14745336

32. Casavilla FA, Marsh JW, Iwatsuki S, et al. Hepatic resection and transplantation for peripheral cholangiocarcinoma. J Am Coll Surg. Nov 1997; 185(5): 429-36. PMID 9358085

33. Ziogas IA, Giannis D, Economopoulos KP, et al. Liver Transplantation for Intrahepatic Cholangiocarcinoma: A Meta-analysis and Meta-regression of Survival Rates. Transplantation. Oct 01 2021; 105(10): 2263-2271. PMID 33196623

34. Hue JJ, Rocha FG, Ammori JB, et al. A comparison of surgical resection and liver transplantation in the treatment of intrahepatic cholangiocarcinoma in the era of modern chemotherapy: An analysis of the National Cancer Database. J Surg Oncol. Mar 2021; 123(4): 949-956. PMID 33400841

35. Palaniappan V, Li CH, Frilling A, et al. Long-Term Outcomes of Liver Transplantation for the Management of Neuroendocrine Neoplasms: A Systematic Review. J Pers Med. Sep 23 2023; 13(10). PMID 37888039

36. Fan ST, Le Treut YP, Mazzaferro V, et al. Liver transplantation for neuroendocrine tumour liver metastases. HPB (Oxford). Jan 2015; 17(1): 23-8. PMID 24992381

37. Máthé Z, Tagkalos E, Paul A, et al. Liver transplantation for hepatic metastases of neuroendocrine pancreatic tumors: a survival-based analysis. Transplantation. Mar 15 2011; 91(5): 575-82. PMID 21200365

38. Adam R, Piedvache C, Chiche L, et al. Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial. Lancet. Sep 21 2024; 404(10458): 1107-1118. PMID 39306468

39. Hagness M, Foss A, Line PD, et al. Liver transplantation for nonresectable liver metastases from colorectal cancer. Ann Surg. May 2013; 257(5): 800-6. PMID 23360920

40. Dueland S, Syversveen T, Solheim JM, et al. Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases. Ann Surg. Feb 2020; 271(2): 212-218. PMID 31188200

41. Dueland S, Yaqub S, Syversveen T, et al. Survival Outcomes After Portal Vein Embolization and Liver Resection Compared With Liver Transplant for Patients With Extensive Colorectal Cancer Liver Metastases. JAMA Surg. Jun 01 2021; 156(6): 550-557. PMID 33787838

42. Larson EL, Ciftci Y, Jenkins RT, et al. Outcomes of Liver Transplant for Hepatic Epithelioid Hemangioendothelioma. Clin Transplant. Feb 2025; 39(2): e70087. PMID 39869081

43. Rodriguez JA, Becker NS, O'Mahony CA, et al. Long-term outcomes following liver transplantation for hepatic hemangioendothelioma: the UNOS experience from 1987 to 2005. J Gastrointest Surg. Jan 2008; 12(1): 110-6. PMID 17710508

44. Lerut JP, Orlando G, Adam R, et al. The place of liver transplantation in the treatment of hepatic epitheloid hemangioendothelioma: report of the European liver transplant registry. Ann Surg. Dec 2007; 246(6): 949-57; discussion 957. PMID 18043096

45. Ziogas IA, Tasoudis PT, Serifis N, et al. Liver Transplantation for Hepatic Adenoma: A UNOS Database Analysis and Systematic Review of the Literature. Transplant Direct. Feb 2022; 8(2): e1264. PMID 35018302

46. Hamilton EC, Balogh J, Nguyen DT, et al. Liver transplantation for primary hepatic malignancies of childhood: The UNOS experience. J Pediatr Surg. Oct 12 2017. PMID 29108844

47. Barrena S, Hernandez F, Miguel M, et al. High-risk hepatoblastoma: results in a pediatric liver transplantation center. Eur J Pediatr Surg. Jan 2011; 21(1): 18-20. PMID 20938901

48. Malek MM, Shah SR, Atri P, et al. Review of outcomes of primary liver cancers in children: our institutional experience with resection and transplantation. Surgery. Oct 2010; 148(4): 778-82; discussion 782-4. PMID 20728194

49. Browne M, Sher D, Grant D, et al. Survival after liver transplantation for hepatoblastoma: a 2-center experience. J Pediatr Surg. Nov 2008; 43(11): 1973-81. PMID 18970927

50. Czauderna P, Otte JB, Aronson DC, et al. Guidelines for surgical treatment of hepatoblastoma in the modern era--recommendations from the Childhood Liver Tumour Strategy Group of the International Society of Paediatric Oncology (SIOPEL). Eur J Cancer. May 2005; 41(7): 1031-6. PMID 15862752

51. Organ Procurement and Transplantation Network (OPTN). Policy 9: Allocation of Livers and Liver-Intestines. Updated June 26, 2025; **https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_01**. Accessed October 13, 2025.

52. Salimi J, Jafarian A, Fakhar N, et al. Study of re-transplantation and prognosis in liver transplant center in Iran. Gastroenterol Hepatol Bed Bench. 2021; 14(3): 237-242. PMID 34221263

53. Bellido CB, Martínez JM, Artacho GS, et al. Have we changed the liver retransplantation survival?. Transplant Proc. 2012; 44(6): 1526-9. PMID 22841203

54. Remiszewski P, Kalinowski P, Dudek K, et al. Influence of selected factors on survival after liver retransplantation. Transplant Proc. Oct 2011; 43(8): 3025-8. PMID 21996216

55. Hong JC, Kaldas FM, Kositamongkol P, et al. Predictive index for long-term survival after retransplantation of the liver in adult recipients: analysis of a 26-year experience in a single center. Ann Surg. Sep 2011; 254(3): 444-8; discussion 448-9. PMID 21817890

56. Bouari S, Rijkse E, Metselaar HJ, et al. A comparison between combined liver kidney transplants to liver transplants alone: A systematic review and meta-analysis. Transplant Rev (Orlando). Dec 2021; 35(4): 100633. PMID 34098490

57. Lunsford KE, Bodzin AS, Markovic D, et al. Avoiding Futility in Simultaneous Liver-kidney Transplantation: Analysis of 331 Consecutive Patients Listed for Dual Organ Replacement. Ann Surg. May 2017; 265(5): 1016-1024. PMID 27232249

58. Fong TL, Khemichian S, Shah T, et al. Combined liver-kidney transplantation is preferable to liver transplant alone for cirrhotic patients with renal failure. Transplantation. Aug 27 2012; 94(4): 411-6. PMID 22805440

59. Ruiz R, Jennings LW, Kim P, et al. Indications for combined liver and kidney transplantation: propositions after a 23-yr experience. Clin Transplant. 2010; 24(6): 807-11. PMID 20002463

60. Calinescu AM, Wildhaber BE, Poncet A, et al. Outcomes of combined liver-kidney transplantation in children: analysis of the scientific registry of transplant recipients. Am J Transplant. Dec 2014; 14(12): 2861-8. PMID 25274400

61. de la Cerda F, Jimenez WA, Gjertson DW, et al. Renal graft outcome after combined liver and kidney transplantation in children: UCLA and UNOS experience. Pediatr Transplant. Jun 2010; 14(4): 459-64. PMID 20070563

62. Marcos A, Ham JM, Fisher RA, et al. Single-center analysis of the first 40 adult-to-adult living donor liver transplants using the right lobe. Liver Transpl. May 2000; 6(3): 296-301. PMID 10827229

63. Malagó M, Testa G, Marcos A, et al. Ethical considerations and rationale of adult-to-adult living donor liver transplantation. Liver Transpl. Oct 2001; 7(10): 921-7. PMID 11679994

64. Renz JF, Busuttil RW. Adult-to-adult living-donor liver transplantation: a critical analysis. Semin Liver Dis. 2000; 20(4): 411-24. PMID 11200412

65. Bak T, Wachs M, Trotter J, et al. Adult-to-adult living donor liver transplantation using right-lobe grafts: results and lessons learned from a single-center experience. Liver Transpl. Aug 2001; 7(8): 680-6. PMID 11510011

66. Shiffman ML, Brown RS, Olthoff KM, et al. Living donor liver transplantation: summary of a conference at The National Institutes of Health. Liver Transpl. Feb 2002; 8(2): 174-88. PMID 11862598

67. Grant RC, Sandhu L, Dixon PR, et al. Living vs. deceased donor liver transplantation for hepatocellular carcinoma: a systematic review and meta-analysis. Clin Transplant. 2013; 27(1): 140-7. PMID 23157398

68. Tang W, Qiu JG, Cai Y, et al. Increased Surgical Complications but Improved Overall Survival with Adult Living Donor Compared to Deceased Donor Liver Transplantation: A Systematic Review and Meta-Analysis. Biomed Res Int. 2020; 2020: 1320830. PMID 32908865

69. Cooper C, Kanters S, Klein M, et al. Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS. Mar 27 2011; 25(6): 777-86. PMID 21412058

70. Terrault NA, Roland ME, Schiano T, et al. Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection. Liver Transpl. Jun 2012; 18(6): 716-26. PMID 22328294

71. Organ Procurement and Transplantation Network (OPTN). Organ Procurement and Transplantation Network Policies. Updated June 26, 2025; **https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf**. Accessed October 13, 2025.

72. Blumberg EA, Rogers CC. Solid organ transplantation in the HIV-infected patient: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. Sep 2019; 33(9): e13499. PMID 30773688

73. Durand CM, Massie A, Florman S, et al. Safety of Kidney Transplantation from Donors with HIV. N Engl J Med. Oct 17 2024; 391(15): 1390-1401. PMID 39413376

74. American Association for the Study of Liver Diseases, American Society of Transplantation. Liver transplantation, evaluation of the adult patient. 2014; **https://www.aasld.org/practice-guidelines/evaluation-adult-liver-transplant-patient**. Accessed October 13, 2025.

75. Squires RH, Ng V, Romero R, et al. Evaluation of the pediatric patient for liver transplantation: 2014 practice guideline by the American Association for the Study of Liver Diseases, American Society of Transplantation and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Hepatology. Jul 2014; 60(1): 362-98. PMID 24782219

76. American Association for the Study of Liver Diseases. Diagnosis and Treatment of Alcohol Associated Liver Diseases: 2019 Practice Guidance From the American Association for the Study of Liver Diseases. **https://www.aasld.org/practice-guidelines/alcohol-associated-liver-disease**. Accessed October 13, 2025.

77. Singal AG, Llovet JM, Yarchoan M, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. Dec 01 2023; 78(6): 1922-1965. PMID 37199193

78. Taddei TH, Brown DB, Yarchoan M, et al. Critical Update: AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. Jul 01 2025; 82(1): 272-274. PMID 39992051

79. Clavien PA, Lesurtel M, Bossuyt PM, et al. Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report. Lancet Oncol. Jan 2012; 13(1): e11-22. PMID 22047762

80. Kodali S, Kulik L, D'Allessio A, et al. The 2024 ILTS-ILCA consensus recommendations for liver transplantation for HCC and intrahepatic cholangiocarcinoma. Liver Transpl. Jun 01 2025; 31(6): 815-831. PMID 40014003

81. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 2.2025. **https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf**. Accessed October 13, 2025.

82. Guidance to Liver Transplant Programs and the National Liver Review Board for: Adult MELD Exceptions for Transplant Oncology (July 2025): Accessed September 10, 2025.

83. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Adult Liver Transplantation (260.1). 2012;**https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=70&ncdver=3**. . Accessed October 13, 2025.

84. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Pediatric Liver Transplantation (260.2). 1991; **https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=71**. Accessed October 13, 2025.

85. Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011;365(19):1790-800. PMID: 22070476.

86. Im GY, Kim-Schluger L, Shenoy A, et al. Early liver transplantation for severe alcoholic hepatitis in the United States-A single- center experience. Am J Transplant 2016;16(3): 841-849. PMID:26710309.

87. Lee BP, Mehta N, Platt L, Gurakar A, et al. Outcomes of early liver transplantation for patients with severe alcoholic hepatitis. Gastroenterology. 2018;155(2):422-430. e1. PMID: 29655837.

88. Weeks SR, Sun Z, McCaul ME, et al. Liver transplantation for severe alcoholic hepatitis, updated lessons from the world's largest series. J Am Coll Surg. 2018;226(4):549-557. PMID:29409981.

89. Marot A, Dubois M, Trépo E et al. Liver transplantation for alcoholic hepatitis: A systematic review with meta-analysis. PLoS One. 2018;13(1): e0190823. PMID:29324766.

90. Friedman SL. Liver transplantation for alcohol-associated liver disease. In: UpToDate, Robson, KM (Ed), UpToDate, Waltham, MA, Last updated September 30, 2025. Accessed October 14, 2025.

91. Louvet A, Naveau S, Abdelnour M, et al. The Lille model: a new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. Hepatology 2007;45(6):1348-54. PMID:17518367.

92. Singal AK, Bataller R, Ahn J, et al. ACG clinical guideline: Alcoholic liver disease. AM J Gastroenterol. 2018 Feb;113(2):175-194. PMID: 29336434.

93. Al-Saeedi M, Barout M, Probst P, et al. Meta-analysis of patient survival and rate of alcohol relapse in liver-transplanted patients for acute alcoholic hepatitis. Langenbecks Arch Surg. 2018; 403 (7):825-836. PMID: 30349998

94. Asrani S, Trotter J, Lake J, et al. Meeting Report: The Dallas consensus conference on liver transplantation for alcohol related hepatitis. Liver Transpl. 2020; 26(1): 127-140. PMID: 31743578.

95. Ayyala-Somayajula D, Han H, TErrault NA. Selective use of liver transplantation for severe alcohol-associated hepatitis. Expert Rev Gastroentrol Hepatol 2020; 14(3):175-184. PMID:32077333.

96. Herrrick-Reynolds KM, Punchhi G, Greenberg RS, et al. Evaluation of early vs. standard liver transplant for alcohol-associated livers disease. JAMA Surg. 2021; 156 (11):1026-1034. PMID: 34379106.

97. Cotter TG, Sandikçi B, Paul S, et al. Liver transplantation for alcoholic hepatitis in the United States: Excellent outcomes with profound temporal and geographic variation in frequency. Am J Transplant 2021; 21(3): 1039-1055. PMID: 32531107.

98. Louvet A, Labreuche J, Moreno C, et al. Early liver transplantation for severe alcohol-related hepatitis not responding to medical treatment: a prospective controlled study. Lancet Gastroenterol Hepatol. 2022;7(5):416-425. PMID: 35202597.

99. Morales Arraez D, Ventura Cots M, Altamirano J, et al., The MELD score is superior to Maddrey's discriminant function score to predict short-term mortality in alcohol-associated hepatitis: a global study. Am J Gastroenterol. 2022;117(2): 301-310. PMID: 34962498.

100. Jophlin LL, Singal AK, Bataller R, et al.ACG Clinical Guideline: Alcohol-Associated Liver Disease. AM J Gastroenterol. 2024; 119(1): 30-54. PMID: 38174913.

# Appendix

## Lille Protocol

Severe acute alcoholic hepatitis defined as Maddrey's discriminant function > 32. Calculation available at: **https://www.mdcalc.com/maddreys-discriminant-function-alcoholic-hepatitis** Accessed October 14, 2025.

- Non-responsive to medical therapy defined as a Lille model [77] score > 0.45 or more after 7 days of medical therapy. Calculation available at: **https://www.mdcalc.com/lille-model-alcoholic-hepatitis** Accessed October 14, 2025.
    - Medical therapy consists of standard medical care for liver insufficiency and use of glucocorticoids (40 mg per day of prednisolone for at least 7 days); **OR**
    - As a continuous increase in the Model for End-Stage Liver Disease (MELD) score
- Severe alcoholic hepatitis as the first liver-decompensating event
- Presence of close supportive family members
- Absence of severe coexisting or psychiatric disorders
- Agreement by individuals (with support from family members) to adhere to lifelong total abstinence
- Selection process consists of 4 medical teams who independently meet the individual and family members
    - Team 1: (closest to the individual): nurses, one resident, one fellow
    - Team 2: specialist in addiction
    - Team 3: senior hepatologists
    - Team 4: anesthesiologist and transplant surgeon
- The 4 evaluating teams have to reach complete consensus on selection

**Source:** Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011;365(19):1790-800. PMID: 22070476.

## History

| Date | Comments |
|---|---|
| 07/01/02 | Add to Surgery Section - New Policy. Replaces other transplant policies (PR.7.03.100, 102, 103, 104, 105, and 106) |
| 05/13/03 | Replace Policy - Scheduled review. References added and CPT code table updated. |
| 01/01/04 | Replace Policy - CPT code updates only. |
| 05/11/04 | Replace Policy - Policy reviewed by Nancy Aceto no changes needed at this time; new review date only. Appendices removed—no value. |
| 09/01/04 | Replace Policy - Policy renumbered from PR.7.03.109. No changes to dates. |
| 05/10/05 | Replace Policy - Scheduled review. References added. No change to policy statement. |
| 02/06/06 | Codes updated - No other changes. |
| 05/09/06 | Replace Policy - Scheduled review. References added; no change to policy statement. |
| 05/26/06 | Scope and Disclaimer Updates - No other changes. |
| 02/26/07 | Codes Updated - No other changes. |
| 05/08/07 | Replace Policy - Policy updated with literature review; reference added. No change in policy statement. |
| 05/21/07 | References Updated - Policy updated with information on Medicare coverage of heart transplants. |
| 05/13/08 | Replace Policy - Policy updated with literature search. Policy statement to include using a cadaver or living donor under kidney transplants as a medically necessary indication. Also to include "imminent end-stage liver failure" for patients under liver transplants as medically necessary. |
| 03/10/09 | Replace Policy - Policy updated with literature search; references added. No change to policy statement. |
| 02/09/10 | Replace Policy - Policy updated with literature search. No change to policy statement. |
| 01/11/11 | Replace Policy - Policy updated with literature search. No change to policy statement. |
| 01/06/12 | Replace Policy – Policy updated with literature search; references added. No change to policy statement. |
| 12/03/12 | Update title to Related Policy 7.03.11. |
| 01/29/13 | Replace policy. Policy updated with literature search. No change to policy statement. References updated. |
| 02/12/13 | Update Related Policies, change title for 8.02.02. |
| 05/30/13 | Update Related Policies. Change title for 7.03.510. |

| Date | Comments |
|---|---|
| 02/10/14 | Replace policy. Retransplant policy statements added to kidney, heart, heart/lung. Literature updated. References 35-39 added. ICD-9 Diagnosis codes were listed for informational purposes only and have been removed from the policy. |
| 03/11/14 | Coding Update. Codes 33.50, 33.51, 33.52, 33.6, 37.5, 50.4, 50.51, 50.59, 52.80, 52.81, 52.82, 52.83, and 55.69 were removed per ICD-10 mapping project; these codes are not utilized for adjudication of policy. |
| 03/31/15 | Annual Review. Alphabetized names of organ transplants in policy statements. Related policy 7.03.05 added. Rationale section extensively reorganized by alphabetizing organ transplants and updated based on a literature review through December, 2014. References extensively renumbered and some references removed. Policy statements unchanged. |
| 08/19/15 | Update Related Policies. Remove 7.03.510 and 8.02.02 then add 8.03.05 and 7.03.04. |
| 09/24/15 | Coding update. ICD-9 Procedure codes removed; these are informational only. |
| 01/12/16 | Annual Review. Policy updated with literature search; references added. No change to the policy statement. |
| 01/29/16 | Coding update. Added HCPCS code S2152. |
| 11/01/16 | Update related policies. Removed 7.03.05 from related policies section as it was deleted (contents moved to 7.03.04). |
| 01/01/17 | Coding Update. Transplant benefit-related codes removed. Coding table moved to Policy Guidelines section. Updated titles of some Related Policies. |
| 03/01/17 | Annual Review, approved February 14, 2017. Policy updated with literature review through October 25, 2016; references renumbered. Policy statements unchanged. |
| 04/14/17 | Coding update; added HCPCS code S2060. |
| 04/18/17 | Coding update; added HCPCS code S2065. |
| 09/01/17 | Policy moved to new format. No changes to policy statement. |
| 07/27/18 | Coding update; added CPT 33935 to policy as it was inadvertently removed. |
| 11/01/18 | Annual Review, approved October 26, 2018. Policy updated with literature review through June 2018; references 42, 51, 56, 82, 87, 89, 94, 109, 111, 118, 120,136, 158, 164, 178,183, 184, and 201 added. Examples of end-stage cardiac and pulmonary diseases added for clarity under heart and lung transplant. Etiologies of end-stage liver disease added for clarity, polycystic disease of the liver, unresectable hilar cholangiocarcinoma, pediatric patients with nonmetastatic hepatoblastoma are added as medically necessary indications for liver transplantation. Indications for liver retransplantation were added. Indications where liver transplantation is not medically necessary or is considered investigational were added, otherwise policy statements unchanged. |
| 04/01/19 | Minor update, added Documentation Requirements section. |

| Date | Comments |
|---|---|
| 11/01/19 | Annual Review approved October 8, 2019. Policy title changed from "Solid Organ Transplants" to "Liver Transplant and Combined Liver-Kidney Transplant". Previous content of Solid Organ Transplants is now addressed in individual policies (7.03.01, 7.03.02, 7.03.07, 7.03.08, 7.03.09) except for liver and combined liver-kidney transplant. Policy updated with literature review through June 2019. References added. Added exception criteria for patients with ongoing alcohol abuse. Added policy statement on transplantation of HCV viremic organs which is taken from BCBSA policy 7.03.14. |
| 04/01/20 | Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020. |
| 06/10/20 | Interim Review, approved June 9, 2020, effective June 10, 2020. This policy is reinstated immediately and will no longer be deleted or replaced with InterQual criteria on July 2, 2020. |
| 11/01/20 | Annual Review, approved October 22, 2020. Policy updated with literature review through July 2020; references added. Policy statements unchanged. |
| 11/01/21 | Annual Review, approved October 5, 2021. Policy updated with literature review through July 6, 2021; references added. Policy statements unchanged. |
| 11/01/22 | Annual Review, approved October 24, 2022. Policy updated with literature review through June 27, 2022; references added and updated. Minor editorial refinements to policy statements; intent unchanged. |
| 11/01/23 | Annual Review, approved October 9, 2023. Policy updated with literature review through June 13, 2023; references added and updated. Removed the policy statement regarding the transplantation of HCV-viremic solid organs to an HCV non-viremic recipient combined with direct-acting antiviral treatment for HCV is considered investigational. Other minor editorial refinements to policy statements made for clarity; intent unchanged. |
| 11/01/24 | Annual Review, approved October 7, 2024. Policy updated with literature review through July 9, 2024; references added. Policy statements unchanged. |
| 12/01/25 | Annual Review, approved November 11, 2025. Policy updated with literature review through July 23, 2025; references added. Policy statements updated to include the indications unresectable colorectal liver metastases, hepatic epithelioid hemangioendothelioma, hepatic adenomas, and intrahepatic cholangiocarcinoma as investigational for liver transplant. |

**Scope**: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.