Referral for Liver Transplantation

This is a PDF version of the following document:
Module 3: Management of Cirrhosis-Related Complications
Lesson 5: Referral for Liver Transplantation

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Background

Liver Transplantation in the United States

Liver transplantation is a life-saving surgery for persons with acute and chronic liver diseases. In the United States, the major disorders that may result in consideration for liver transplantation include acute liver failure, chronic liver disease with advanced cirrhosis, hepatocellular carcinoma (HCC), and liver-based metabolic defects.[1,2] In the United States, in 2022 there were 9,257 liver transplants performed.[2] From 1988 through 2022, the overall trend was a steady increase in the number of liver transplants performed in the United States, with a 50% increase in transplants during the years 2012 (Figure 1).[2,3,4] Advances in the field of transplantation have improved post-primary liver transplant survival rates in the United States to 91.8% at 1 year after liver transplantation, 83.3% at 3 years, and 76.1% at 5 years.[5,6] This review will discuss general information and principles regarding liver transplantation, with a focus on specific information related to liver transplantation for persons with hepatitis C virus (HCV)

Liver Transplantation in Persons with Chronic HCV Infection

For more than a decade, chronic HCV infection was the most common indication for liver transplantation in the United States, but alcohol-related liver disease is now a more common indication than chronic HCV (Figure 2).[3,7,8] This change reflects both the rise in alcohol-related liver disease and the effectiveness of direct-acting antiviral (DAA) drugs to treat HCV. In the early DAA era, the number of people on the waiting list due to HCV-related complications decreased by 32% in the United States.[9] Since acute HCV rarely causes liver failure, nearly all transplants related to HCV involve persons with chronic HCV infection who have developed cirrhosis-related complications. Data from 2012-2014 for persons with chronic HCV monoinfection who received a liver transplant in the United States showed that most recipients were male (70.8%) and White (69.1%).[10] During this time period, among the 41,557 persons listed for orthotopic liver transplantation, 21,064 (51.2%) received a liver transplant.[10]

Indications for Liver Transplantation

Indications for Liver Transplantation

The 2013 AASLD/AST Evaluation for Liver Transplantation Guidelines state that “liver transplant is indicated when the limits of medical therapy have been reached.”[11] The 2013 AASLD/AST Evaluation for Liver Transplantation Guidelines outline four major types of indications for liver transplantation in the United States: (1) acute liver failure, (2) complications of cirrhosis, (3) liver-based metabolic diseases, and (4) systemic complications of chronic liver disease.[11] In addition, there are some rare conditions that can warrant liver transplantation (Figure 3).[1,2] The following briefly summarizes the major indications for liver transplantation.

Acute Liver Failure

Acute liver failure is defined as the development of hepatic encephalopathy (any degree of mental alteration) and coagulopathy (international normalized ratio [INR] greater than or equal to 1.5) within 26 weeks from the onset of symptoms related to acute hepatitis in persons without preexisting liver disease.[12] Common causes of acute liver failure include acetaminophen overdose, acute viral hepatitis, drug-induced liver injury, mushroom poisoning, autoimmune hepatitis, Wilson's disease, acute ischemic hepatitis (shock liver), and acute fatty liver of pregnancy.[11,12,13,14,15] Acute HCV infrequently causes acute liver failure. Individuals who meet the criteria for acute liver failure should be urgently transferred to a liver transplant center for transplant evaluation and for intensive management of liver failure.[12] Given the rapidity of clinical deterioration, these candidates receive a special priority listing category (Status 1) for deceased donor organs.[11]

Cirrhotic Liver Disease with Complications

In the United States, chronic liver diseases that cause cirrhosis are by far the most common indication for liver transplantation. Alcohol-related liver disease, metabolic dysfunction-associated steatotic liver disease (previously termed nonalcoholic fatty liver disease), and chronic HCV infection are the most common disorders that lead to cirrhosis and require liver transplantation (Figure 4).[3] The major cirrhosis-related reasons for transplantation include the development of (1) a decompensating event or condition, such as ascites, hepatic encephalopathy, or variceal hemorrhage, (2) hepatocellular dysfunction with a Model for End-Stage Liver Disease that incorporates serum sodium level (MELD-Na) score of 15 or greater, and (3) HCC within transplant criteria.[11] In the United States, HCV infection with cirrhosis is the most common cause of HCC.[16] Although HCC can be cured in some instances with hepatic resection and locoregional therapy, most individuals who have HCC confined to the liver should be considered for liver transplant.[17,18] For example, persons with HCC who meet Milan criteria (solitary HCC lesion less than 5 cm or up to 3 nodules smaller than 3 cm) and have no radiographic evidence of extrahepatic disease, but who are not candidates for surgical resection, are considered liver transplantation candidates, and granted priority for liver transplantation.[19,20] Certain persons with liver tumor burdens in excess of the Milan criteria may undergo HCC treatment as part of a down-staging protocol in an effort to become eligible as liver transplant candidates.[21] Some centers consider liver transplantation for select individuals with HCC exceeding Milan criteria.[22]

Metabolic Conditions

Liver transplantation is also considered for those with metabolic diseases, such as familial amyloidosis, Wilson's disease, glycogen storage disease, hemochromatosis, primary hyperoxaluria, and alpha-1 antitrypsin deficiency.[23,24,25,26,27,28] Many of these metabolic diseases originate in the liver but may require liver transplantation because of severe systemic symptoms.[1,11] Other less common metabolic causes include urea cycle defects, branched-chain amino acid disorders, tyrosinemia, and homozygous familial hypercholesterolemia.[1]

Systemic Complications for Chronic Liver Disease

Two major systemic complications of liver disease that may require liver transplantation are hepatopulmonary syndrome and portopulmonary syndrome.

- **Hepatopulmonary Syndrome**: The hepatopulmonary syndrome is characterized by underlying liver disease and/or portal hypertension that leads to pulmonary microvascular dilatation, pulmonary shunting, and reduced arterial oxygenation.[29,30] Individuals with a room air pulse oximetry SpO2 less than 96% at sea level should be further evaluated for hepatopulmonary syndrome by contrast echocardiography or ^{99m}TC macroaggregated albumin (MAA) lung-brain perfusion scanning. There are no known effective medical treatments for hepatopulmonary syndrome, and liver transplantation remains the only approach to reverse this condition, with estimated 5-year survival rates of approximately 75%—a marked improvement over supportive medical therapy alone.[29,31,32,33]
- **Portopulmonary Hypertension**: Portopulmonary hypertension is a severe local hypertensive complication that can result from pulmonary vasoconstriction in persons with cirrhosis and portal hypertension; portopulmonary hypertension can progress to right heart failure and death.[29,34] Liver transplantation is not a first-line option for most persons with portopulmonary hypertension, since moderate to severe portopulmonary hypertension is associated with increased post-transplant mortality, but it can be considered in selected situations, if pulmonary artery pressures have been lowered to less than 35 mm Hg and pulmonary vascular resistance is reduced to less than 400 dunes/sec/cm^{-5} with vasodilator therapy.[35,36]

Rare Indications

Other rare conditions for which liver transplantation is considered include fibrolamellar HCC, hepatic epithelioid hemangioendothelioma, hereditary hemorrhagic telangiectasia, hepatoblastoma, neonatal hemochromatosis, metastatic neuroendocrine tumors, erythropoietic protoporphyria, and polycystic liver disease. There are some centers with approved protocols for performing liver transplantation in persons with early-stage unresectable hilar cholangiocarcinoma, in combination with neoadjuvant chemoradiation therapy.[37]

Timing for Cirrhosis-Related Liver Transplantation

The need for liver transplantation in a person with chronic HCV infection is almost always because of a cirrhosis-related complication. Thus, the following discussion will focus on the timing for liver transplantation in persons who have cirrhosis-related complications. When considering referral for liver transplantation, the natural history of the disease should be compared against the expected survival after transplantation. The use of prognostic scoring systems can assist in this consideration by predicting survival among persons with cirrhosis. Individuals who have an indication for liver transplantation should ideally be referred early in the clinical course because the transplant evaluation may take weeks to months to complete.

Decompensated Cirrhosis

Decompensated cirrhosis is defined by the occurrence of a complication, such as ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, or hepatorenal syndrome. The development of decompensated cirrhosis negatively influences prognosis.[38] In a natural history study in persons with cirrhosis, more than 90% with compensated cirrhosis were still alive after 5 years, compared with only 50% survival at 5 years among those who experienced a decompensating event.[39] Moreover, once decompensation occurred, 20% died within one year. Similar findings have been repeated in other studies. Accordingly, persons with cirrhosis should be referred for transplant evaluation when they experience their first major cirrhosis-related complication, such as ascites, variceal bleeding, or hepatic encephalopathy.[1,11]

Use of Prognostic Scoring Systems

Scoring systems that were initially designed to predict outcomes following portocaval shunt surgery and transjugular intrahepatic portosystemic shunts (TIPS) have been used to predict overall survival in persons with cirrhosis.

- **Model for End-Stage Liver Disease (MELD)**: The prognostic MELD has been shown to be a useful tool in predicting short-term survival in persons with chronic liver disease, and MELD has become the most important indicator for transplantation. It uses a continuous scale from 6 to 40 based on serum bilirubin, international normalized ratio (INR) of prothrombin time, and serum creatinine.[40,41] The modified MELD score was shown to predict mortality for persons on the liver transplant waiting list and was implemented in February 2002, replacing the Child-Turcotte-Pugh score, to prioritize persons for donor allocation in the United States (Figure 5).[42] A similar model, Pediatric End-Stage Liver Disease (PELD), is used for children and adolescents.[43] In January 2016, the MELD scoring system for donor allocation in the United States was further modified to incorporate serum sodium, using the MELD-Na equation (see the MELD Calculator Tool); the serum sodium is incorporated only for persons with a MELD score greater than 11.[44] In July 2023, the MELD 3.0, which further incorporates serum albumin and female sex, was implemented.[45] The MELD 3.0 contains three new features: (1) two variables (female sex and serum albumin) were added to the equation, (2) the serum creatinine ceiling was lowered from 4.0 mg/dL to 3.0 mg/dL, and (3) two interaction terms (between albumin and creatinine and between bilirubin and sodium) were included.[45] Based on current guidelines, individuals with a MELD score (or MELD 3.0) of 15 or greater should be referred to a liver transplant center for evaluation.
- **Child-Turcotte-Pugh (CTP)**: The CTP classification (Figure 6) can be used to predict short-term prognosis in persons awaiting transplantation.[46,47,48] Individuals with a CTP score of 7 to 9 (class B) have an estimated 1-year survival of 80%.[49] In the past, a CTP score of 7 or greater was considered a minimal listing criteria for liver transplantation.[50] For the purpose of listing criteria for liver transplantation, the CTP score is no longer used, and it has been replaced by the MELD score.

Urgent Transplantation Referral for Persons with Cirrhosis

Individuals with cirrhosis and type 1 acute kidney injury-hepatorenal syndrome have a median survival of less

than 2 weeks and should be urgently referred to a transplant center for an expedited transplant evaluation, as should those with other evidence for rapid hepatic decompensation.[1,11]

Contraindications to Liver Transplantation

Absolute Contraindications

Candidates for transplant surgery need to be able to survive the surgery and the immediate postoperative period, be adherent with taking the post-transplant medical regimen, and not have comorbid conditions that could limit graft or patient survival, particularly those that could significantly worsen by the use of immunosuppressive medications. Specific contraindications for liver transplantation vary across transplant centers. The 2013 AASLD/AST Evaluation for Liver Transplantation Guidelines list the following as contraindications for liver transplantation:[11]

- MELD Score less than 15
- Severe cardiac or pulmonary disease
- AIDS
- Ongoing alcohol or illicit substance use
- Hepatocellular carcinoma with metastatic spread
- Uncontrolled sepsis
- Anatomic abnormality that precludes liver transplantation
- Intrahepatic cholangiocarcinoma
- Extrahepatic malignancy
- Fulminant hepatic failure with sustained intracranial pressure greater than 50 mm Hg or cerebral perfusion pressure less than 40 mm Hg
- Hemangiosarcoma
- Persistent noncompliance
- Lack of adequate social support system

Relative Contraindications

Some medical providers have the misperception that chronic HCV or older age are relative contraindications to liver transplantation. Advanced cirrhosis from chronic HCV infection is one of the leading indications for liver transplantation worldwide and an important underlying cause for liver transplantation in the United States.[1] Hepatitis C treatment can be pursued before or after liver transplantation, with timing to be determined based on clinical guidance. There is no age cutoff for liver transplantation, but older persons have poorer long-term survival due to an increased risk of death from malignancies. Some notable relative contraindications for liver transplantation are listed below.[11]

- **Coronary Artery Disease**: Individuals with risk factors for coronary artery disease or known history of coronary artery disease require more thorough investigation. Cardiac revascularization may be needed in candidates with significant coronary artery stenosis.
- **Cigarette Smokers:** Individuals who have a history of smoking, and especially those who continue to smoke have decreased post-transplant survival due to increased risks of cardiac death and malignancies, including oropharyngeal cancers.
- **Chronic or Recurrent Infections**: Individuals with chronic or recurrent infections should be evaluated by a transplant infectious diseases specialist. Persons with HIV should be referred to select transplant centers with expertise in managing potential drug interactions between antiretroviral drugs and the immunosuppression regimen. Typically, candidates with HIV will need to have CD4 counts consistently above 100 cells/mm^3 and a suppressed HIV RNA level by the time of liver transplantation.
- **Extrahepatic Malignancies**: Individuals with extrahepatic malignancies are at risk of recurrent disease due to the use of long-term immunosuppression after transplantation. Typically, transplant centers may request a reasonable waiting period after cure of a malignancy (except for nonmelanoma skin cancers) before considering transplantation, although there is no consensus on the optimal window of time needed.
- **Portal Vein Thrombosis**: Although portal venous thrombosis is common and does not preclude

transplant for most people, transplantation may not be a viable option if there is absence of a viable splanchnic venous inflow system, such as a patent large mesenteric or collateral vessel to use.

- **Body Mass Index**: Short- and long-term survival is decreased in persons at extremes of body mass index (less than 18.5 kg/m^2 or greater than or equal to 40 kg/m^2).
- **Psychiatric Disorders**: Significant psychiatric disorders must be well controlled to optimize compliance after transplantation.
- **Alcohol or Substance Use Disorders:** Individuals with a history of alcohol and/or substance use disorders are often required to have a period of abstinence for consideration of liver transplant candidacy, and some centers may require counseling and/or attendance in treatment programs for relapse prevention and assurance of compliance with the post-transplant regimen. Persons undergoing liver transplantation need to have adequate support from family and/or friends to assist through the evaluation and the perioperative period. There are an increasing number of centers that also consider liver transplantation in highly selected patients with severe alcoholic hepatitis who fail to respond to medical therapy.[51,52]

Finding Information About Liver Transplant Centers

Scientific Registry of Transplant Recipients (SRTR)

The Scientific Registry of Transplant Recipients (SRTR) provides statistical and other analytic support to the Organ Procurement and Transplantation Network (OPTN) and generates analytic data to support the United States Health and Human Services (HHS) in activities related to solid organ transplantation.[7] The SRTR site includes a function to find and compare transplant programs, as well as information about waiting list numbers and transplant activity, waiting list mortality rates, transplant numbers and rates, and survival statistics for all transplant centers. In addition, the site information includes a summary page listing one-year post-transplant survival rates, grading them as higher than expected, as expected, or lower than expected based on risk adjustment models.

Organ Procurement and Transplantation Network (OPTN)

In 1984, the United States Congress enacted the National Organ Transplant Act (NOTA) and established the Organ Procurement and Transplantation Network (OPTN); the purpose of the 1984 act was to create a unified transplant network to be operated by a private, non-profit organization under federal contract. The initial contract for the OPTN was awarded to the United Network for Organ Sharing (UNOS) in 1986, and since that time, UNOS has administered the OPTN. The OPTN maintains the national liver transplantation waiting list, manages transplant policies, and provides support and informational services for individuals, all of which can be found on the OPTN website.

United Network for Organ Sharing (UNOS)

The United Network for Oran Sharing (UNOS) is a private, non-profit organization located in Richmond, Virginia, that works under contract with the federal government to manage the United States organ transplant system, including operation of the Organ Procurement and Transplantation Network (OPTN). Specific UNOS activities include managing the national transplant waiting list, matching donors to recipients, and maintaining a database that includes information for all transplant events that take place in the United States.

Transplantation Evaluation

The transplantation evaluation process is focused on the assessment of operative risks, medical compliance, and comorbid conditions that could affect overall survival and graft survival, especially in the context of long-term immunosuppressive therapy.[1,11] The specific evaluation process varies across different transplant centers but typically will include assessments by a transplant hepatologist, a social worker, and a transplant surgeon, in addition to other staff. A multidisciplinary selection committee then reviews the evaluation to determine if the individual needs to be listed for a liver transplant listing and if they are a viable candidate. This committee may make requests for further evaluation or interventions needed before transplant candidacy is accepted. Once approved, individuals are listed on the donor organ waiting list based on their ABO blood type, with priority established by the MELD 3.0 score, except for persons with acute liver failure who demand the highest priority, as Status 1. Liver transplantation candidates are eligible for simultaneous kidney transplantation if they have any of the following:[53]

- A diagnosis of chronic kidney disease with glomerular filtration rate (GFR) less than or equal to 60 mL/min for more than 90 consecutive days and either end-stage renal disease on dialysis or a GFR less than or equal to 30 mL/min; *or*
- Sustained acute kidney injury and at least one of the following for the last 6 weeks: dialysis at least once weekly or GFR less than or equal to 25 mL/min documented at least once weekly; *or*
- A diagnosis of metabolic disease with at least one of the following: hyperoxaluria, atypical hemolytic uremic syndrome from mutations in factor H or factor I, familial non-neuropathic systemic amyloidosis, or methylmalonic aciduria.

As a safety net, certain liver transplant recipients who were not offered simultaneous liver and kidney transplantation at the start and who remain dialysis-dependent after transplant are highly prioritized for subsequent kidney-alone offers.[53]

Initial Transplantation Evaluation

The information below summarizes the key elements typically assessed in the transplantation evaluation.

- **Financial Screening**: Obtain medical insurance approval first for transplant evaluation
- **Hepatology Evaluation**: Conduct a thorough history and physical examination, and optimize management of the underlying liver condition
- **Laboratory Testing**: Obtain the following baseline laboratory studies.
    - Hepatic function panel (including total bilirubin and albumin), electrolytes, renal function, complete blood counts
    - Viral hepatitis profiles (A, B, C)
    - Serologic studies for herpesviruses (cytomegalovirus, Epstein-Barr virus, and herpes simplex virus)
    - Diagnostic tests for HIV infection
    - Screening for nonviral infections (syphilis, toxoplasmosis)
    - Screening for latent tuberculosis (QuantiFERON-TB Gold assay or purified protein derivative skin test)
    - Markers for other causes of liver disease (e.g., anti-nuclear antibody [ANA], anti-smooth muscle antibody, anti-mitochondrial antibody, and iron studies)
    - Tumor markers (e.g., alpha-fetoprotein)
    - Urinalysis and urine drug screen, 24-hour urine for creatinine clearance
    - ABO-Rh blood typing
- **Cardiopulmonary Evaluation**: Obtain pulse oximetry, electrocardiography, and echocardiography; if indicated, perform pulmonary function testing, cardiac stress testing, and/or cardiac catheterization.
- **Abdominal Imaging**: Evaluate hepatic artery anatomy, portal vein anatomy, and screen for hepatocellular carcinoma using dynamic contrast imaging (CT or MRI) or ultrasonography with

Doppler. If hepatocellular carcinoma is present, then dynamic contrast imaging (CT or MRI) is needed to assess the size and number of lesions and evaluate for vascular invasion and extrahepatic spread.

- **General Health Assessment**: Obtain chest radiograph, bone density assessment, dental evaluation, vaccinations, esophagogastroduodenoscopy, and age or condition-appropriate cancer screening.
- **Dietitian Evaluation**: Assess nutritional status and dietary recommendations.
- **Social Work Evaluation**: Assess psychosocial status and address care support needs.
- **Psychiatry or Psychology Evaluation**: Review history of psychiatric and/or substance use disorders, if present.
- **Anesthesia Evaluation**: Review cardiopulmonary and anesthesia risks and history of complications.
- **Transplant Surgery Evaluation**: Review technical aspects and risks of surgery, and discuss donor options.
- **Infectious Disease Evaluation**: Assess for infections that may require treatment prior to transplant and guide post-transplant surveillance in the setting of immunosuppression.
- **Financial Counseling**: Develop financial management plans for the surgery and post-transplantation care.

Summary Points

- In the United States, in recent years, approximately 9,000 to 10,000 liver transplantations are performed annually, and chronic HCV infection is the second most common indication for transplantation.
- Persons with cirrhosis should be referred for a liver transplant evaluation if any of the following criteria are met: (1) MELD score is greater than or equal to 15, (2) complication due to cirrhosis (e.g., ascites, variceal hemorrhage, or hepatic encephalopathy), or (3) diagnosis of hepatocellular carcinoma within Milan criteria (solitary HCC lesion less than 5 cm or up to 3 nodules each smaller than 3 cm).
- Additional indications for liver transplantation include (1) persons with acute liver failure (INR greater than or equal to 1.5 and hepatic encephalopathy), presenting within 26 weeks from the onset of symptoms, without preexisting liver disease, (2) persons with liver-based metabolic defects with significant systemic manifestations, or (3) systemic complications of chronic liver failure.
- Transplant candidacy is dependent upon the person’s ability to survive transplant surgery and the immediate postoperative period, the person’s ability to comply with the post-transplant medical regimen, and the absence of comorbid conditions that could increase the risk of graft rejection or adversely impact survival, particularly those conditions that could be worsened by the use of immunosuppression.
- There are multiple contraindications to liver transplantation, and these include absolute and relative contraindications. Certain criteria may vary amongst different transplant centers, but all transplant centers in the United States adhere to OPTN transplant policies.
- Given the time required to complete the transplant evaluation, potential transplant candidates should be referred earlier rather than later in the course of the disease.

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Figures

Figure 1 Liver Transplants in United States, 1988-2022

Source: OPTN/SRTR Annual Data Reports: Liver. Scientific Registry of Transplant Recipients. U.S. Department of Health and Human Resources

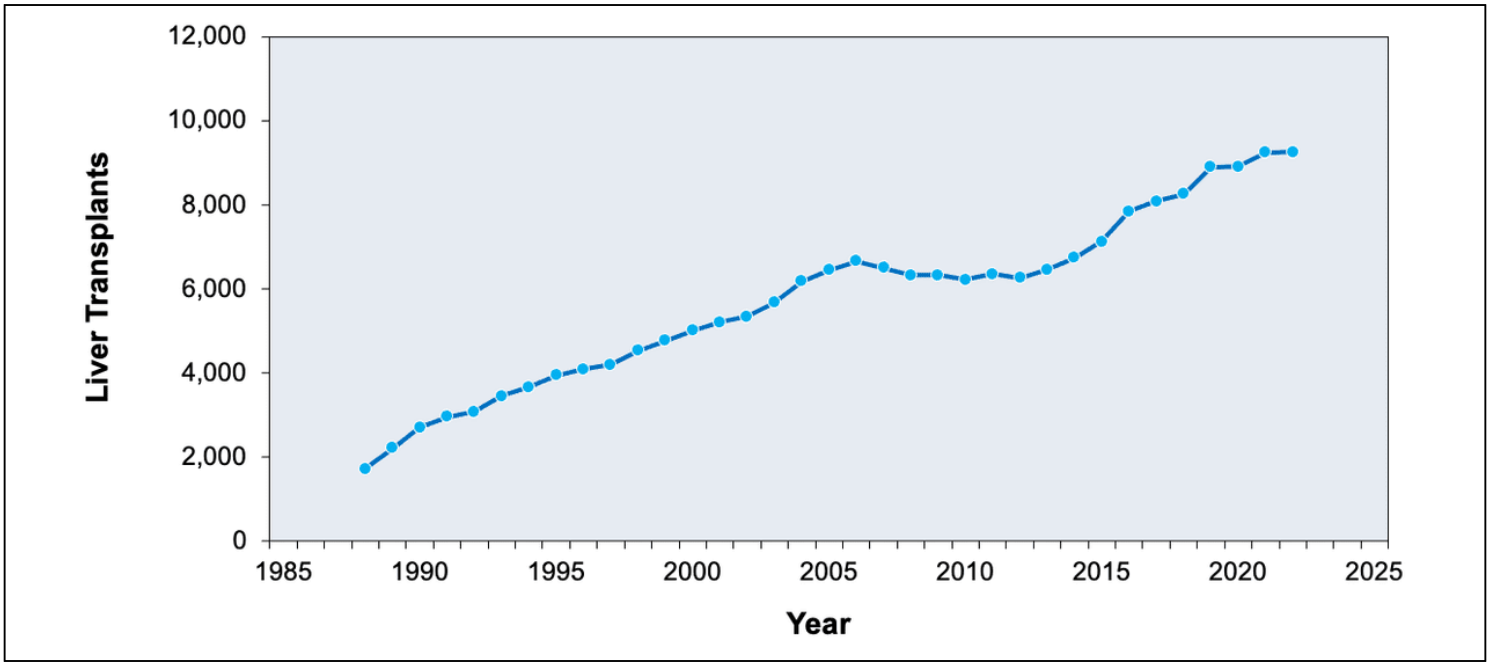

Figure 2 Hepatitis C Virus and Alcoholic Liver Disease as Indication for Adult Liver Transplant Recipients, 2012 and 2022

This graphic compares chronic hepatitis C virus (HCV) and alcoholic liver disease as the indication for liver transplantation in persons receiving a liver transplantation in 2012 versus those in 2022.

Source: Kwong AJ, Kim WR, Lake JR, et al. OPTN/SRTR 2022 Annual Data Report: Liver. Scientific Registry of Transplant Recipients. U.S. Department of Health and Human Resources

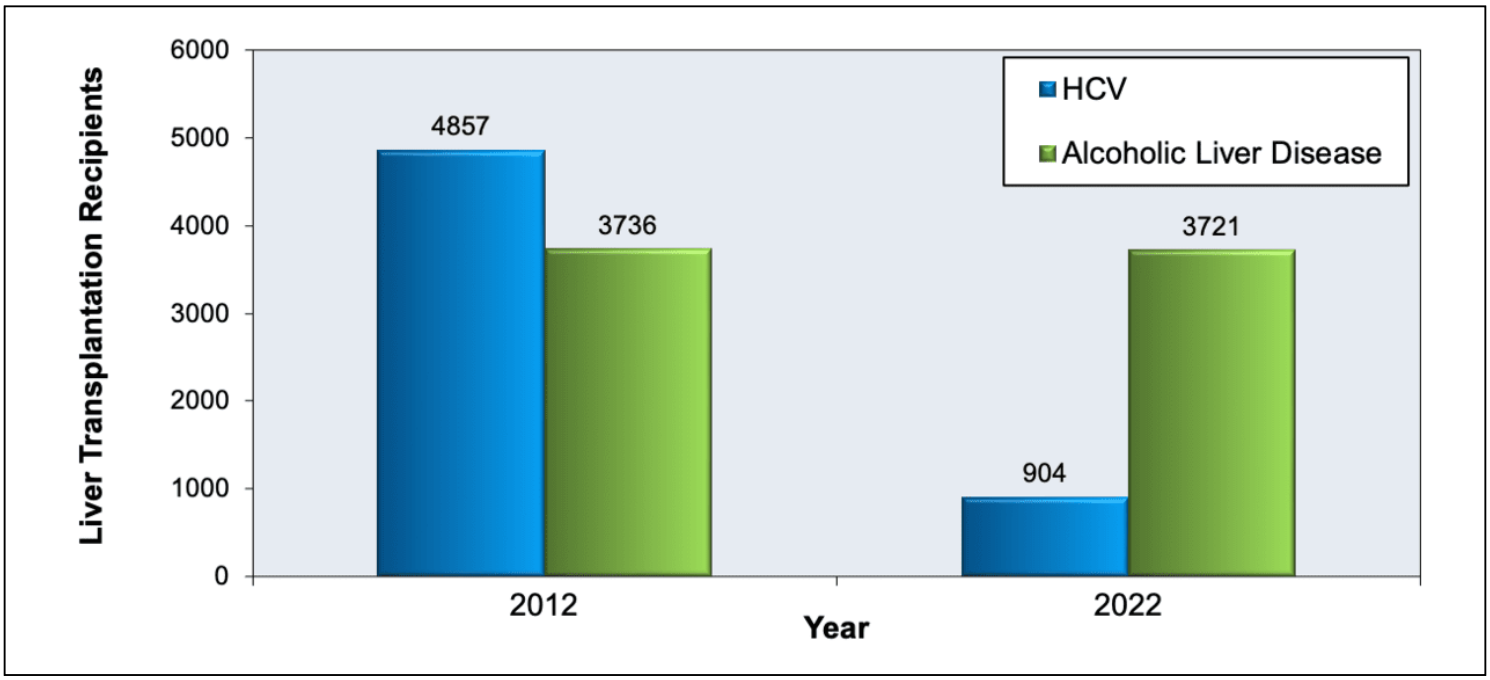

Figure 3 Indications for Liver Transplantation Evaluation

This table shows the major indications for liver transplantation in adults. The most common reason for liver transplantation is cirrhosis from chronic liver disease.

Source: O'Leary JG, Lepe R, Davis GL. Indications for liver transplantation. Gastroenterology. 2008. 134;1764-76.

Indications for Liver Transplantation	
Acute Liver Failure	**Metabolic Disorders Originating from the Liver**
Acute viral hepatitis	Hyperoxaluria
Drug- or toxin-induced hepatotoxicity	Familial Amyloidosis
Acetaminophen overdose	Urea cycle defects
Autoimmune hepatitis	Branched-chain amino acid disorders
Wilson's disease	Familial homozygous hypercholesterolemia
Cirrhosis from Chronic Liver Disease	**Malignancies**
Chronic viral hepatitis	Hepatocellular carcinoma
Alcoholic liver disease	Cholangiocarcinoma (limited)
Autoimmune hepatitis	Hepatoblastoma
Cholestatic liver disease	Fibrolamellar hepatocellular carcinoma
Wilson's disease	Metastatic neuroendocrine tumors
Hereditary and neonatal hemochromatosis	Hemangioendothelioma
Alpha-1-antitrypsin deficiency	**Miscellaneous**
Non-alcoholic steatohepatitis	Polycystic liver disease
Cryptogenic liver disease	Hereditary hemorrhagic telangiectasia
Budd-Chiari syndrome	Erythropoietic protoporphyria
Tyrosinemia	
Glycogen storage diseases	

Figure 4 Clinical Characteristics of Adult Liver Transplant Recipients, 2022

Source: Kwong AJ, Kim WR, Lake JR, et al. OPTN/SRTR 2022 Annual Data Report: Liver. Scientific Registry of Transplant Recipients. U.S. Department of Health and Human Resources

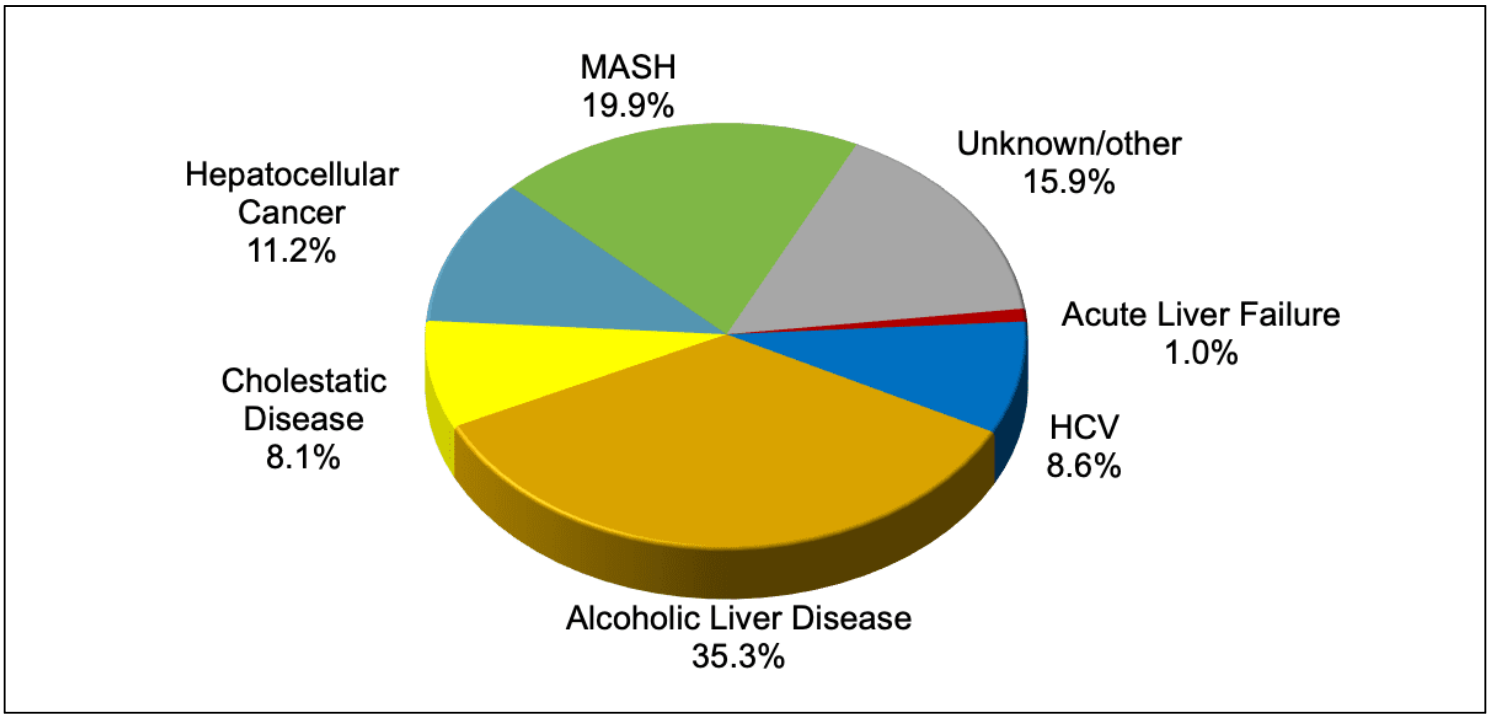

Figure 5 Correlation of MELD Score and 3-Month Survival

The cohort of patients in this study included adults (at least 18 years of age) with chronic liver disease who were added to the Organ Procurement Transplantation Network (OPTN) waiting list at a 2A or 2B status. This graphic shows a clear association of MELD score and 3-month survival. Those with a MELD score of 40 or greater had a mortality rate of 71% at 3 months.

Source: Wiesner R, Edwards E, Freeman R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology. 2003;124:91-6.

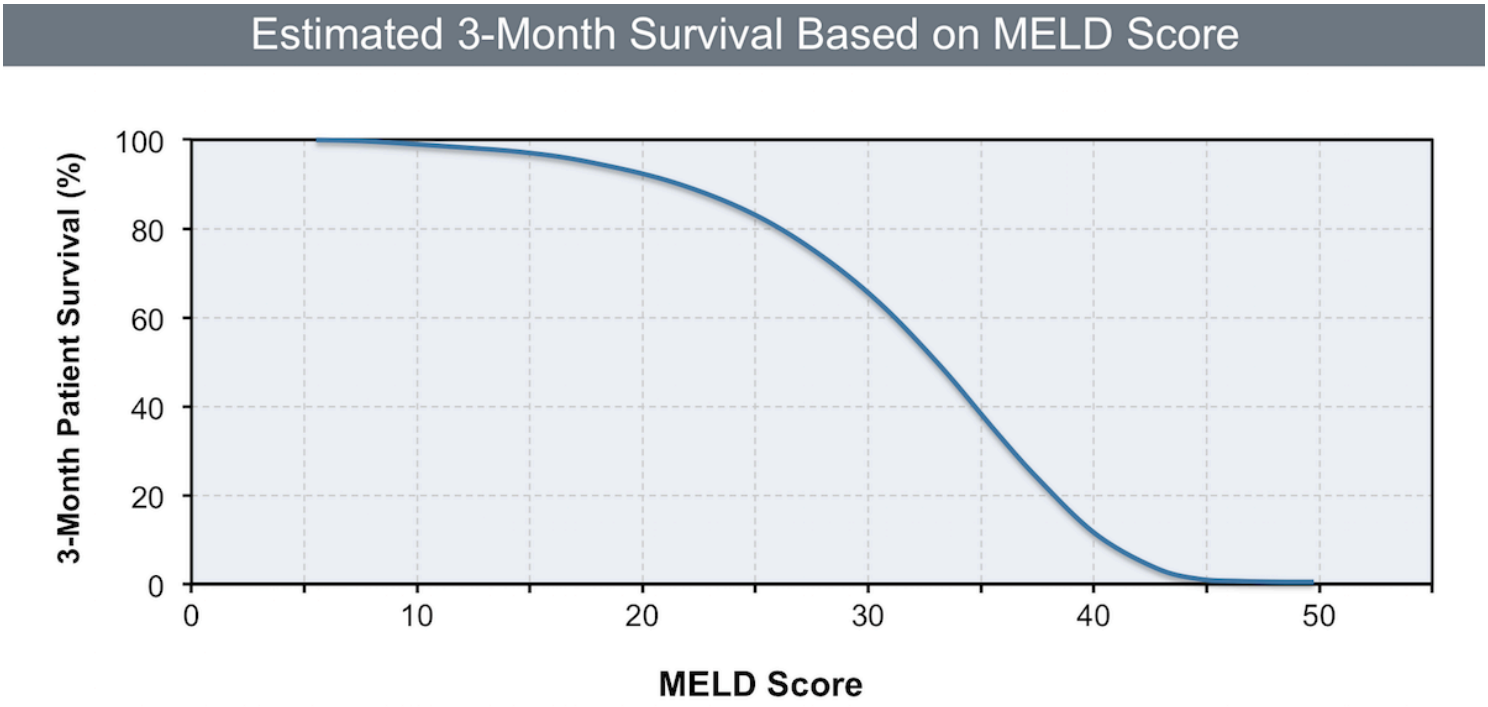

Figure 6 Child-Turcotte-Pugh Classification for Severity of Liver Disease

The Child-Turcotte-Pugh (CTP) classification system utilizes two clinical parameters (encephalopathy and ascites) and three laboratory values (bilirubin, albumin, and prothrombin time). Patients are classified as class A, B, or C based on their total points.

Source: Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973;60:646-9.

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	**Points***		
	1	2	3
Encephalopathy	None	Grade 1 or 2	Grade 3 or 4
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
or			
International normalized ratio	<1.7	1.7-2.3	>2.3
***Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)**			
Class A = 5 to 6 points			
Class B = 7 to 9 points			
Class C = 10 to 15 points			