

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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Indications for Liver Transplantation

Liver transplantation is a life-saving surgery for patients with acute and chronic liver diseases. The major disorders that may result in consideration for liver transplantation include acute liver failure, chronic liver disease with advanced cirrhosis, hepatocellular carcinoma, and liver-based metabolic defects ([Figure 1](#)).^[1] In 2015, more than 7,000 liver transplants were performed in the United States, and chronic hepatitis C virus (HCV) infection was the most common indication for the transplantation. Advances in the field of transplantation have improved post-transplant survival rates in the United States to 87.7% at one year after liver transplantation, 79.9% at 3 years, and 74.3% at 5 years.^[2]

Acute Liver Failure

Acute liver failure is the development of hepatic encephalopathy and coagulopathy (international ionized ratio [INR] greater than or equal to 1.5) within 26 weeks from the onset of symptoms related to acute hepatitis (e.g. jaundice) in patients without pre-existing liver disease. Causes of acute liver failure include acetaminophen overdose, acute viral hepatitis, drug-induced liver injury, autoimmune hepatitis, and fatty liver of pregnancy. These patients should be urgently transferred to a liver transplant center for acute care. Liver transplantation should be considered in patients with poor prognosis or low probability of spontaneous recovery. Given the rapidity of clinical deterioration, these candidates receive a special listing category (Status 1) to prioritize for deceased donor organs. Acute infection with hepatitis C virus rarely causes acute liver failure and thus is a very rare indication for liver transplantation.

Cirrhotic Liver Disease

Chronic liver diseases that cause cirrhosis are by far the most common indication for liver transplantation in the United States. Specific chronic liver diseases that can lead to cirrhosis include chronic viral hepatitis (e.g. hepatitis B and hepatitis C), autoimmune hepatitis, alcoholic liver disease, cholestatic liver diseases (e.g. primary biliary cirrhosis, primary sclerosing cholangitis, and cystic fibrosis), metabolic disorders (e.g. alpha-1-antitrypsin deficiency, Wilson disease, non-alcoholic steatohepatitis, and hereditary hemochromatosis), and vascular disorders (e.g. Budd-Chiari syndrome).

Hepatocellular Carcinoma (HCC)

Patients with cirrhosis are at risk for developing hepatocellular carcinoma. The highest risk of HCC is in those with hereditary hemochromatosis, chronic hepatitis B, and chronic hepatitis C, with incidence rates estimated at around 2 to 8% per year. In the United States, hepatitis C with cirrhosis is the most common cause of HCC and HCC was the leading indication for liver transplantation in

2015.[3] Hepatic resection is considered a treatment option for patients with HCC and compensated cirrhosis without significant portal hypertension,[4] but more than 50% who undergo hepatic resection will develop recurrence of HCC within 5 years.[5] The same risk of recurrent HCC results from locoregional therapy, such as radiofrequency ablation, percutaneous ethanol injection, and chemoembolization. Early experience with transplantation of unresectable HCCs demonstrated a high rate of early recurrence and limited survival. Later analysis, however, has demonstrated improved results for transplantation limited to patients who meet Milan criteria (solitary HCC lesion less than 5 cm or up to 3 nodules smaller than 3 cm).[6] Patients with HCC who meet Milan criteria 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.[7] In an attempt to match the risk of death in patients with decompensated cirrhosis, the MELD score is automatically adjusted to a MELD exception score of 22 for initial listing; the score is then increased every 3 months while on the transplant waiting list to reflect a corresponding 10% increase in mortality for each 3-month interval that transpires.[8] The 1-year and 5-year post-transplant survival rates for patients with tumors meeting Milan criteria are 89% and 61%, respectively, which are considered acceptable rates.[7] Certain transplantation centers in the United States have expanded transplant criteria (HCC that does not meet Milan criteria or downstaging of HCC through neoadjuvant locoregional therapy to within the Milan criteria) that may provide a patient consideration for transplantation under investigational or specialized protocols.

Other Conditions

Liver transplantation is also considered for those with metabolic diseases originating in the liver with severe extrahepatic manifestations, such as amyloidosis, hyperoxaluria, urea cycle defects, and branched-chain amino acid disorders. Other rare conditions for which liver transplantation is considered include fibrolamellar HCC, hemangioendothelioma, hereditary hemorrhagic telangiectasia, hepatoblastoma, neonatal hemochromatosis, tyrosinemia, glycogen storage disease, homozygous familial hypercholesterolemia, metastatic neuroendocrine tumors, erythropoietic protoporphyria, polycystic liver disease, and cholangiocarcinoma (under investigation in certain transplant centers.)

Timing for Liver Transplantation

When considering referral for liver transplantation, the natural history of the disease should be compared against the expected survival after transplantation. Patients who have an indication for liver transplantation should ideally be referred early in the clinical course rather than late because the transplant evaluation may take weeks to months to complete.

Use of Prognostic Scoring Systems

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

- **Child-Turcotte-Pugh (CTO):** The CTP classification ([Figure 2](#)) can be used to predict short-term prognosis ([Figure 3](#)) in patients awaiting transplantation.[\[9,10,11\]](#) Patients with a CTP score of 7 to 9 (class B) have an estimated 1-year survival of 80%.[\[12\]](#) In the past, a CTP score of 7 or greater was considered a minimal listing criteria for liver transplantation.[\[13\]](#)
- **Model for End-Stage Liver Disease (MELD):** The prognostic MELD has been shown to be a useful tool in predicting short-term survival in patients 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 of prothrombin time (INR), and serum creatinine.[\[14,15\]](#) The modified MELD score (see MELD calculator tool) has been shown to predict mortality for patients on the liver transplant waiting list ([Figure 4](#)) and was implemented in February 2002, replacing CTP score, to prioritize patients for donor allocation in the United States.[\[16\]](#) A similar model, pediatric end-stage liver disease (PELD), is used for pediatric patients.[\[17\]](#) 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; the serum sodium is incorporated in only for patients with a MELD score greater than 11.[\[8\]](#) Based on current guidelines, patients with a MELD score of 15 or greater or a CTP score of 7 or greater should be referred to a liver transplant center for evaluation.

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.[\[18\]](#) In a natural history study in patients with cirrhosis, more than 90% of the patients who remained compensated were still alive at 5 years, compared with only 50% survival at 5 years among those who experienced a decompensating event.[\[19\]](#) Moreover, once decompensation occurred, 20% died within one year. Similar findings have been repeated in other studies. Accordingly, patients should be referred for transplant evaluation when they experience their first major cirrhosis-related complication, such as ascites, variceal bleeding, or hepatic encephalopathy.[\[1,20\]](#)

Urgent Referral for Transplantation

Patients with cirrhosis and type 1 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. In addition, patients diagnosed with hepatopulmonary syndrome or portopulmonary hypertension, attributed to cirrhosis, should be referred for consideration of transplantation. In addition, patients with acute liver failure also should have urgent referral and transfer to a liver transplantation center.[\[1,20\]](#)

Contraindications for Liver Transplantation

Absolute Contraindications

Candidates for transplant surgery need to be able to survive the surgery and the immediate post-operative period, be compliant with the post-transplant medical regimen, and not have co-morbid 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. There are, however, some criteria that are universally considered exclusionary for transplantation ([Figure 5](#)). [1]

Relative Contraindications

Some of the notable relative contraindications are listed below.[20] Some medical providers have the misperception that chronic hepatitis C or older age are relative contraindications to liver transplantation. Advanced cirrhosis from chronic hepatitis C infection is one of the leading indications for liver transplantation worldwide, accounting for around 40% of the transplants in the United States.[1] Recurrence of hepatitis C infection is universal in the absence of treatment but that does not preclude transplantation. There is no age cut-off for liver transplantation, but older patients have poorer long-term survival due to an increased risk of death from malignancies.

- **Coronary Artery Disease:** Patients with risk factors for coronary artery disease or known history of coronary artery disease require more thorough investigation.
- **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.
- **Chronic or Recurrent Infections:** Patients with chronic or recurrent infections should be evaluated by a transplant infectious disease specialist to determine the availability and efficacy of treatment and risk of immunosuppression. Patients with HIV should be referred to select transplant centers with expertise in managing the numerous drug-drug interactions between antiretroviral drugs and the immunosuppression regimen.
- **Extrahepatic Manifestations:** Patients with extrahepatic malignancies are at risk of recurrent disease due to the use of immunosuppression long-term after transplantation.
- **Malignancy:** Typically, transplant centers may request a reasonable waiting period after cure of a malignancy (with the exception of nonmelanomatous skin cancers) before considering transplantation, although there is no consensus on the optimum window of time needed. Liver transplantation for early-stage perihilar cholangiocarcinoma is done at a few centers under investigational protocols with some success in a highly selected group.
- **Portal Vein Thrombosis:** Although portal venous thrombosis is not uncommon, 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 patients at extremes of body mass index (less than 18.5 kg/m² or greater than or equal to 40 kg/m²).
- **Psychiatric Disorders:** Significant psychiatric disorders must be well controlled to optimize compliance after transplantation.
- **Alcohol or Substance Abuse:** Patients with a history of alcohol and/or substance abuse are usually required to have a period of abstinence for consideration of candidacy, and some may require counseling and/or attendance in treatment programs for relapse prevention and assurance of compliance with the post-transplant regimen. Patients need to have adequate support from family and/or friends to assist through the evaluation and the perioperative period.

Finding a Liver Transplantation Center

Scientific Registry of Transplant Recipients (SRTR)

The [SRTR website](#) provides a list of transplant centers near a certain address, city, or postal code. The SRTR site also reports waiting list number and transplant activity, waiting list mortality rates, transplant number and rates, and survival statistics for all transplant centers, including 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 United Network for Organ Sharing (UNOS) in 1986 and since that time UNOS has administered the OPTN. The OPTN maintains the national patient waiting list, manages transplant policies, and provides support and informational services for patients, all of which can be found on the [OPTN website](#).

United Network for Organ Sharing (UNOS)

The [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.

Pre-Transplantation Evaluation

Pretransplantation Evaluation

The pretransplantation evaluation is focused on the assessment of operative risks, medical compliance, and co-morbid conditions that could affect patient and graft survival, especially in the context of immunosuppressive therapy.^[1,21] 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 multi-disciplinary selection committee then reviews the evaluations to determine if the patient is in need of liver transplant listing and is a viable candidate. This committee may make requests for further evaluation or interventions needed before transplant candidacy is accepted. Once approved, patients are listed on the donor organ waiting list based on their ABO blood type, with priority established by the MELD score, either natural or assigned, with the exception of patients with acute liver failure who demand the highest priority as Status 1. 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:** Thorough history and physical examination, optimize management of liver condition
- **Laboratory Testing:**
 - Hepatic synthetic function, electrolytes, renal function, complete blood counts
 - Viral hepatitis profiles (A,B,C,D)
 - Serologic studies for herpesviruses (cytomegalovirus, Epstein-Barr virus, and herpes simplex virus)
 - Testing for HIV infection
 - Screening for non-viral 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. ANA, ASMA, AMA, iron studies, etc)
 - Tumor markers (e.g. alpha-fetoprotein)
 - Urinalysis and urine drug screen, 24h urine for creatinine clearance
 - ABO-Rh blood typing
- **Cardiopulmonary Evaluation:** Obtain electrocardiography and echocardiography; if indicated, perform pulmonary function testing, cardiac stress testing, and cardiac catheterization
- **Abdominal Imaging:** Evaluation of hepatic artery and portal vein anatomy and screening for hepatocellular carcinoma using dynamic contrast imaging (CT or MRI) or ultrasonography with Doppler
- **General Health Assessment:** Chest radiograph, bone density assessment, dental evaluation, vaccinations, esophagogastroduodenoscopy, age or condition-appropriate cancer screening
- **Dietician 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 abuse disorders, if present
- **Anesthesia Evaluation:** Review cardiopulmonary and anesthesia risks and history of complications
- **Transplant Surgery Evaluation:** Review technical aspects and risks of surgery
- **Financial Counseling:** Develop financial management plans for the surgery and post-transplantation

Summary Points

- In the United States, more than 8,000 liver transplantations are performed annually and chronic hepatitis C infection is the most common indication.
- Patients with cirrhosis should be referred to a liver transplant center for evaluation if any of the following criteria are met: (a) MELD score is greater than or equal to 15 or CTP score is greater than or equal to 7, (b) patients experience their first complication due to cirrhosis (e.g. ascites, variceal hemorrhage, or hepatic encephalopathy), or (c) diagnosis of hepatocellular carcinoma within Milan criteria (solitary HCC lesion less than 5 cm or up to 3 nodules each smaller than 3 cm).
- Patients with acute liver failure or liver-based metabolic defects with significant extrahepatic effects also should be considered for liver transplantation.
- Transplant candidacy is dependent upon the patient's ability to survive transplant surgery and the immediate post-operative period, the patient's ability to comply with the post-transplant medical regimen, and the absence of co-morbid conditions that could limit graft or patient survival, particularly those that could be worsened by the use of immunosuppression.
- Absolute contraindications to liver transplantation are active extrahepatic malignancy, significant extrahepatic infection, hepatocellular carcinoma with macrovascular invasion or extrahepatic spread, severe cardiopulmonary disease, and active substance and/or alcohol abuse.
- Given the time required to complete the transplant evaluation, patients should be referred earlier rather than later in the course of the disease.

Citations

1. O'Leary JG, Lepe R, Davis GL. Indications for liver transplantation. *Gastroenterology*. 2008;134:1764-76.
[\[PubMed Abstract\]](#) -
2. Thuluvath PJ, Krok KL, Segev DL, Yoo HY. Trends in post-liver transplant survival in patients with hepatitis C between 1991 and 2001 in the United States. *Liver Transpl*. 2007;13:719-24.
[\[PubMed Abstract\]](#) -
3. Yang JD, Larson JJ, Watt KD, et al. Hepatocellular Carcinoma Is the Most Common Indication for Liver Transplantation and Placement on the Waitlist in the United States. *Clin Gastroenterol Hepatol*. 2017;15:767-775.e3.
[\[PubMed Abstract\]](#) -
4. Cha CH, Ruo L, Fong Y, Jarnagin WR, Shia J, Blumgart LH, DeMatteo RP. Resection of hepatocellular carcinoma in patients otherwise eligible for transplantation. *Ann Surg*. 2003;238:315-21.
[\[PubMed Abstract\]](#) -
5. Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. *Hepatology*. 2011;53:1020-2.
[\[AASLD Practice Guidelines\]](#) -
6. 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*. 1996;334:693-9.
[\[PubMed Abstract\]](#) -
7. Pelletier SJ, Fu S, Thyagarajan V, et al. An intention-to-treat analysis of liver transplantation for hepatocellular carcinoma using organ procurement transplant network data. *Liver Transpl*. 2009;15:859-68.
[\[PubMed Abstract\]](#) -
8. Kalra A, Wedd JP, Biggins SW. Changing prioritization for transplantation: MELD-Na, hepatocellular carcinoma exceptions, and more. *Curr Opin Organ Transplant*. 2016;21:120-6.
[\[PubMed Abstract\]](#) -
9. Child CG, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg*. 1964;1:1-85.
[\[PubMed Abstract\]](#) -
10. Infante-Rivard C, Esnaola S, Villeneuve JP. Clinical and statistical validity of conventional prognostic factors in predicting short-term survival among cirrhotics. *Hepatology*. 1987;7:660-4.
[\[PubMed Abstract\]](#) -
11. 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.
[\[PubMed Abstract\]](#) -
12. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol*. 2006;44:217-31.
[\[PubMed Abstract\]](#) -
13. Lucey MR, Brown KA, Everson GT, et al. Minimal criteria for placement of adults on the liver transplant waiting list: a report of a national conference organized by the American Society of

Transplant Physicians and the American Association for the Study of Liver Diseases. Liver Transpl Surg. 1997;3:628-37.

[[PubMed Abstract](#)] -

14. Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001;33:464-70.
[[PubMed Abstract](#)] -
15. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31:864-71.
[[PubMed Abstract](#)] -
16. 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.
[[PubMed Abstract](#)] -
17. McDiarmid SV, Merion RM, Dykstra DM, Harper AM. Selection of pediatric candidates under the PELD system. Liver Transpl. 2004;10:S23-30.
[[PubMed Abstract](#)] -
18. Ginés P, Quintero E, Arroyo V, et al. Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987;7:122-8.
[[PubMed Abstract](#)] -
19. Fattovich G, Giustina G, Degos F, et al. Morbidity and mortality in compensated cirrhosis type C: a retrospective follow-up study of 384 patients. Gastroenterology. 1997;112:463-72.
[[PubMed Abstract](#)] -
20. Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology. 2014;59:1144-65.
[[PubMed Abstract](#)] -
21. Murray KF, Carithers RL Jr; AASLD. AASLD practice guidelines: Evaluation of the patient for liver transplantation. Hepatology. 2005;41:1407-32.
[[AASLD Practice Guidelines](#)] -

References

- Dienstag JL, Ghany MG, Morgan TR, et al. A prospective study of the rate of progression in compensated, histologically advanced chronic hepatitis C. Hepatology. 2011;54:396-405.
[[PubMed Abstract](#)] -
- Lee WM, Stravitz RT, Larson AM. Introduction to the revised American Association for the Study of Liver Diseases Position Paper on acute liver failure 2011. Hepatology. 2012;55:965-7.
[[PubMed Abstract](#)] -
- Murray KF, Carithers RL Jr; AASLD. AASLD practice guidelines: Evaluation of the patient for liver transplantation. Hepatology. 2005;41:1407-32.
[[AASLD Practice Guidelines](#)] -
- O'Leary JG, Lepe R, Davis GL. Indications for liver transplantation. Gastroenterology. 2008. 134;1764-76.

[\[PubMed Abstract\]](#) -

- Propst A, Propst T, Zangerl G, Ofner D, Judmaier G, Vogel W. Prognosis and life expectancy in chronic liver disease. Dig Dis Sci. 1995;40:1805-15.
[\[PubMed Abstract\]](#) -

- 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.
[\[PubMed Abstract\]](#) -

Figures

Figure 1 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	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 2 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 <i>or</i> International normalized ratio	<4 <1.7	4-6 1.7-2.3	>6 >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			

Figure 3 Child-Turcotte-Pugh Score and Mortality at 3 Months

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. Those with higher baseline Child-Turcotte-Pugh scores have a marked increase in risk of death at 3 months than those with lower Child-Turcotte-Pugh scores.

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.

3-Month Mortality Based on Child-Turcotte-Pugh Score

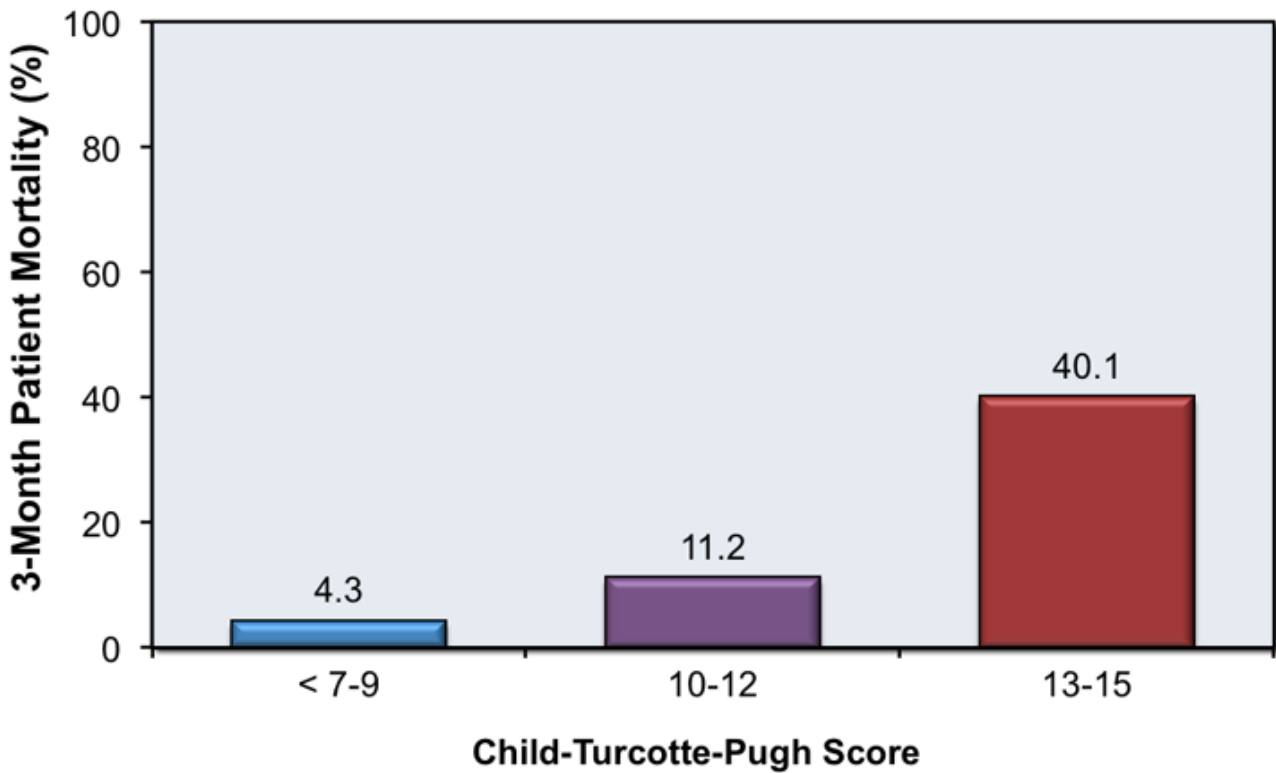


Figure 4 Correlation of MELD Score and 3-Month Survival

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.

3-Month Survival Based on MELD Score

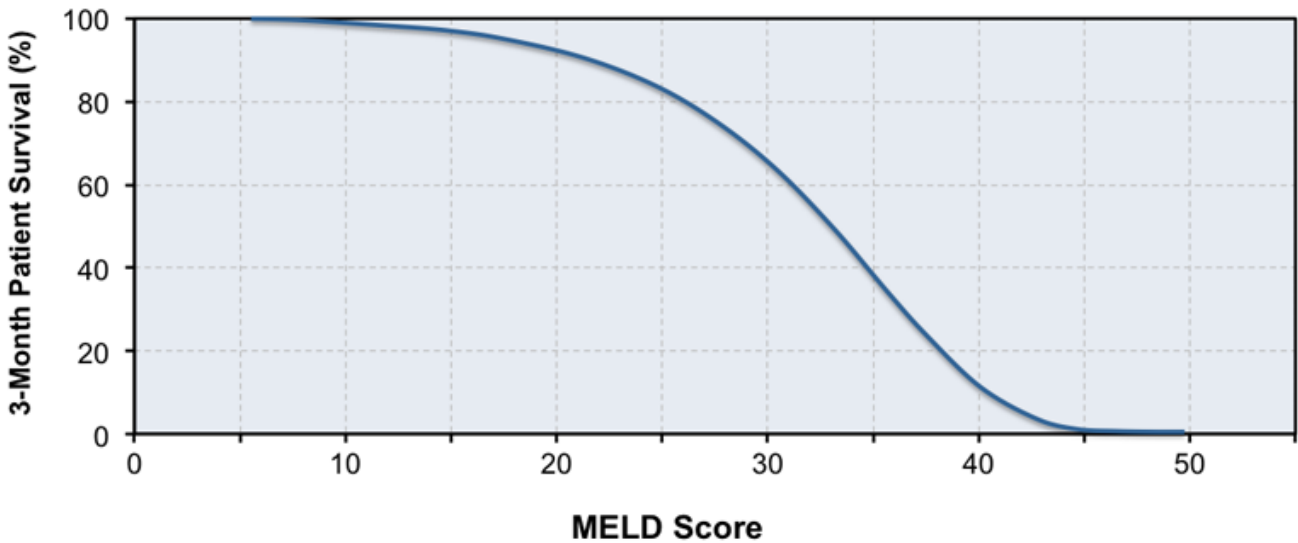


Figure 5 Absolute Contraindications for Liver Transplantation

The list shown here summarizes eight of the most common absolute contraindications for liver transplantation. Note that different transplantation centers have their own criteria for absolute contraindications for liver transplantation.

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

Absolute Contraindications to Liver Transplantation
Active extrahepatic malignancy
Hepatic malignancy with macrovascular invasion or extrahepatic spread
Active and uncontrolled infection outside of the hepatobiliary system
Severe cardiopulmonary disease
Technical and/or anatomical surgical barriers
Brain death
Active substance and/or alcohol abuse
Psychosocial issues that preclude recovery after transplantation