Liver transplantation in adults: Patient selection and pretransplantation evaluation

AUTHORS: Lorna M Dove, MD, MPH, Robert S Brown, Jr, MD, MPH
SECTION EDITOR: Keith D Lindor, MD
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

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INTRODUCTION

Liver transplantation is an important treatment option for patients with acute liver failure, end-stage liver disease, and primary hepatic malignancy, though it is not the initial or primary treatment modality for most liver diseases.

Transplantation infrequently cures the underlying disease; recurrent liver disease after transplantation occurs in 0 to 100 percent of patients, depending on the disease for which transplantation was performed. Thus, the decision to list a patient for transplantation is a risk-benefit analysis in which the inherent risks of surgery, recurrent disease, and long-term immunosuppression must be weighed against the potential benefits of transplantation. These benefits differ for each patient but include improvements in survival, prevention of long-term complications, and better health-related quality of life. In most cases, the risks associated with recurrent disease do not outweigh the benefits of liver transplantation.

This topic will review the selection of patients for liver transplantation and the pretransplantation evaluation. Other issues related to liver transplantation including donor selection, living donor liver transplantation, immunosuppression following liver transplantation, and the medical management of patients who have undergone liver transplantation are discussed elsewhere. (See "Liver transplantation in adults: Deceased donor evaluation and selection" and "Living donor liver transplantation in adults" and "Liver transplantation in adults:

Initial and maintenance immunosuppression" and "Liver transplantation in adults: Long-term management of transplant recipients".)

The American Association for the Study of Liver Diseases and the American Society of Transplantation have developed guidelines regarding the indications for liver transplantation and the evaluation of patients being considered for liver transplantation [1]. The discussion that follows is generally consistent with those guidelines.

FREQUENCY OF LIVER TRANSPLANTATION BY UNDERLYING LIVER DISEASE

According to the United Network for Organ Sharing/Organ Procurement and Transplantation Network registry, hepatocellular carcinoma and hepatitis C virus cirrhosis have been the most common diseases leading to liver transplantation, although increasing numbers of patients with alcoholic cirrhosis and nonalcoholic steatohepatitis are receiving transplants [2,3]. For additional information, see optn.transplant.hrsa.gov/data/view-data-reports.

INDICATIONS

Acute liver failure — Patients with acute liver failure are given the highest priority for liver transplantation (United Network for Organ Sharing [UNOS] status 1). In the absence of liver transplantation, patients with acute liver failure will either have a complete recovery of liver function or will die [4]. However, because it can be difficult to predict whether a given patient will recover, patients with acute liver failure should be referred to a liver transplantation center as soon as possible. (See "Acute liver failure in adults: Management and prognosis", section on 'Liver transplantation'.)

Acute liver failure is defined by the development of severe acute liver injury with encephalopathy and impaired synthetic function (international normalized ratio [INR] of ≥1.5) in a patient without cirrhosis or preexisting liver disease. While the time course that differentiates acute liver failure from chronic liver failure varies between reports, a commonly used cutoff is an illness duration of <26 weeks. While there are numerous causes of acute liver failure (table 1), viral and drug-induced hepatitis are the most common causes of acute liver failure in adults. (See "Acute liver failure in adults: Etiology, clinical manifestations, and diagnosis".)

Cirrhosis — The presence of cirrhosis alone is not sufficient to warrant transplantation. Transplantation is generally considered when a patient has suffered either a complication of portal hypertension or a manifestation of compromised hepatic function [1]. Variceal hemorrhage, ascites, and encephalopathy are the primary manifestations of end-stage liver

disease and are designated as markers of decompensation. The onset of decompensation is associated with significantly impaired survival. Another complication of cirrhosis is the development of hepatorenal syndrome, which is an ominous marker and signals the need for immediate transplantation evaluation. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis".)

Patients with cirrhosis are typically candidates for liver transplantation once their biologic Model for End-stage Liver Disease (MELD) score is ≥15 (MELD-Na score). However, some patients with Child B cirrhosis (table 2) with portal hypertension but a low MELD score may be candidates for liver transplantation. The transplantation evaluation is typically started once a patient has a MELD score >10. This permits the patient to meet the transplantation team prior to the development of end-stage liver disease and ensures adequate time for the patient to complete the pretransplantation evaluation. If patients are referred for evaluation once end-stage liver disease has developed, there may not be adequate time for education, and the patient may have impaired mental status from underlying encephalopathy. (See "Model for End-stage Liver Disease (MELD)", section on 'Prioritization for liver transplantation based on MELD score'.)

Patients may also qualify for liver transplantation if they have a complication or condition that qualifies for standard MELD exception points. Exception points are awarded because there are some conditions associated with chronic liver disease that may result in impaired survival but are not directly accounted for in the MELD scoring system. Conditions that qualify for MELD exception points include (see "Model for End-stage Liver Disease (MELD)", section on 'Standard MELD exceptions in liver transplantation'):

- Hepatocellular carcinoma
- Hepatopulmonary syndrome
- Portopulmonary hypertension (provided the mean arterial pressure can be maintained at <35 mmHg with treatment)
- Familial amyloid polyneuropathy
- Primary hyperoxaluria
- Cystic fibrosis
- Hilar cholangiocarcinoma (provided the liver transplantation center has a UNOS-approved protocol detailing the work-up and management of patients with cholangiocarcinoma undergoing transplantation)
- Hepatic artery thrombosis (occurring within 14 days of liver transplantation but not meeting criteria for status 1A)

Finally, patients may have complicating medical conditions that are related to their liver disease but that do not qualify for standard MELD exception points. Such patients can be considered for liver transplantation if their clinicians believe that the biologic MELD score does not adequately reflect a patient's true liver-related morbidity and mortality or if the complications are severely impairing the patient's quality of life. Some of these complications include (see "Model for End-stage Liver Disease (MELD)", section on 'Petitioning for additional MELD points'):

- Recurrent cholangitis in patients with primary sclerosing cholangitis who are on antibiotic suppressive therapy or require repeated biliary interventions
- Refractory ascites
- Refractory hepatic encephalopathy
- Refractory variceal hemorrhage
- Portal hypertensive gastropathy leading to chronic blood loss
- Intractable pruritus in a patient with primary biliary cirrhosis

Liver neoplasms — Patients with some primary liver neoplasms may be candidates for liver transplantation, provided the neoplasms meet specific criteria (eg, for patients with hepatocellular carcinoma [HCC], a single lesion ≤5 cm or up to three separate lesions all <3 cm, no evidence of gross vascular invasion, and no regional nodal or distant metastases). In addition, there may be a role for liver transplantation in patients with neuroendocrine tumors that have metastasized to the liver, but experience in this setting is limited [5]. (See "Metastatic gastroenteropancreatic neuroendocrine tumors: Local options to control tumor growth and symptoms of hormone hypersecretion", section on 'Liver transplantation'.)

Some of the liver neoplasms that have been treated with liver transplantation include [5]:

- HCC (including fibrolamellar HCC) (see "Liver transplantation for hepatocellular carcinoma" and "Epidemiology, clinical manifestations, diagnosis, and treatment of fibrolamellar carcinoma", section on 'Liver transplantation')
- Epithelioid hemangioendothelioma [6-8]
- Large hepatocellular adenomas (see "Hepatocellular adenoma")

Metabolic disorders — Several liver-based metabolic conditions with systemic manifestations may be treated with liver transplantation. In some cases (eg, alpha-1 antitrypsin deficiency and Wilson disease), patients are cured of the underlying disease with liver transplantation, though some clinical manifestations may not be reversible.

Liver-based metabolic conditions that have been treated with liver transplantation include:

- Familial amyloid polyneuropathy (qualifies for standard MELD exception points) [9-11].

- Primary hyperoxaluria (qualifies for standard MELD exception points) (see "Primary hyperoxaluria", section on 'Transplantation').
- Cystic fibrosis (qualifies for standard MELD exception points) (see "Cystic fibrosis: Hepatobiliary disease", section on 'Management').
- Alpha-1 antitrypsin deficiency [12,13].
- Some forms of glycogen storage disease (type I and type IV) (see "Glucose-6-phosphatase deficiency (glycogen storage disease I, von Gierke disease)", section on 'Liver transplantation' and "Glycogen branching enzyme deficiency (glycogen storage disease IV, Andersen disease)", section on 'Treatment').
- Tyrosinemia (see "Disorders of tyrosine metabolism", section on 'Liver transplantation').
- Hemochromatosis [14,15].
- Wilson disease (see "Wilson disease: Treatment and prognosis").
- Acute intermittent porphyria (see "Acute intermittent porphyria: Management", section on 'Liver transplantation').

In the case of alpha-1 antitrypsin deficiency, cystic fibrosis, tyrosinemia, hemochromatosis, and Wilson disease, liver transplantation is usually reserved for patients who have developed end-stage liver disease or HCC.

CONTRAINDICATIONS

Although organ allocation is centralized, criteria and contraindications to listing for liver transplantation are often transplantation center-specific. General contraindications adopted by most centers include [1]:

- Cardiopulmonary disease that cannot be corrected and is a prohibitive risk for surgery
- Acquired immunodeficiency syndrome (AIDS)
- Malignancy outside of the liver not meeting oncologic criteria for cure
- Hepatocellular carcinoma with metastatic spread
- Hemangiosarcoma
- Anatomic abnormalities that preclude liver transplantation
- Uncontrolled sepsis

- Acute liver failure with a sustained intracranial pressure >50 mmHg or a cerebral perfusion pressure <40 mmHg
- Persistent nonadherence with medical care
- Lack of adequate social support

For patients with alcohol-associated liver disease, some programs require a minimum period of abstinence, participation in a structured rehabilitation and abstinence program, and adequate social support to help maintain sobriety. The six-month period of abstinence is not required by many centers in patients with severe alcohol-associated hepatitis who meet center protocol. Ongoing research is needed to identify transplant candidates who are at low risk of post-transplant relapse. Pretransplant management and post-transplant outcomes for patients with alcohol-associated liver disease are discussed in more detail separately. (See "Liver transplantation for alcohol-associated liver disease" and "Management and prognosis of alcoholic hepatitis", section on 'Liver transplantation'.)

Advanced age and human immunodeficiency virus (HIV) (but not AIDS) are examples of relative contraindications that are site-specific and are often decided on a case-by-case basis. Liver transplantation can be performed in those older than 65 years of age, provided that there has been a comprehensive evaluation for comorbidities [16].

Many transplantation centers in the United States and Europe perform liver transplantation for patients with HIV [17-24]. The available data have suggested favorable outcomes for patients who were not coinfected with hepatitis C virus (HCV) [25-28]. Initial studies on the efficacy of direct-acting antiviral therapy in coinfected patients are promising; therefore, we anticipate that further study will demonstrate similar post-transplant survival rates for HIV/HCV-coinfected patients compared with HCV-monoinfected patients [29,30]. We list patients with HIV for transplantation if they meet other criteria. We do not exclude patients with HCV coinfection because antiviral therapy for HCV improves outcomes following transplantation (see "Hepatitis C virus infection in liver transplant candidates and recipients"). In addition to the standard pretransplantation counseling, patients with HIV have the option of receiving an organ from an HIV-infected donor, according to the HIV Organ Policy Equity Act [31]. (See "Kidney transplantation in adults: Kidney transplantation in patients with HIV", section on 'Donors with HIV'.)

Society guidelines suggest that class 3 obesity (body mass index [BMI] ≥40) is a relative contraindication to liver transplant [1]. However, studies are not conclusive as to whether patients with increased BMI and/or metabolic syndrome have worse outcomes following transplantation [32,33]. Whether all patients with high BMI should be excluded from

transplantation and what cutoff should be used (BMI >40, >50) remains controversial, and some centers will perform a gastric sleeve before or at the time of transplantation [34].

PRETRANSPLANTATION EVALUATION

The goal of the pretransplantation evaluation is to assess the patient's ability to tolerate the stress of surgery, immunosuppression, and the demands of post-transplantation care. Thus, each patient undergoes an extensive cardiopulmonary evaluation, screening for occult infection or cancer, and psychosocial evaluation (table 3). Specific testing varies depending on the patient's age, medical history, and transplantation center practice. In addition, while a certain battery of tests may initiate the work-up, more testing may be indicated if the initial test results are abnormal or if the patient has signs or symptoms of a significant comorbid illness that is not evaluated as part of the initial evaluation.

Laboratory testing — Laboratory tests that should be obtained in patients being evaluated for liver transplantation include:

- ABO-Rh blood typing
- Liver biochemical and function tests (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, international normalized ratio [INR])
- Complete blood count with differential
- Creatinine clearance
- Serum sodium
- Serum alpha-fetoprotein
- Calcium and vitamin D levels
- Serum phosphatidyl ethanol (PEth)
- Serologies for cytomegalovirus, Epstein-Barr virus, varicella, human immunodeficiency virus, hepatitis A, hepatitis B, hepatitis C, rapid plasma reagin (RPR)
- Urinalysis
- Urine drug screen

Cardiopulmonary evaluation — The cardiopulmonary evaluation is designed to evaluate for coronary artery disease, valvular heart disease, cardiomyopathy, obstructive or restrictive lung disease, hepatopulmonary syndrome, and pulmonary hypertension [1,32-37]. However, there is no consensus among liver transplant programs on the optimal strategy for testing. The American Heart Association (AHA) has published a statement with a suggested protocol for coronary heart disease screening in liver transplant [38].

There are some nuances in cardiac evaluation (reduced afterload, hyperdynamic circulation, etc) that need to be taken into account in patients with cirrhosis to ensure that the work-up is appropriately vigorous. Some findings discovered during initial testing may permanently preclude transplantation, whereas others may need to be treated or corrected prior to surgery. Given the complexity, most centers work in close partnership with cardiologists and anesthesiologists knowledgeable in the physiology of cirrhosis and transplant surgery.

Morbidity and mortality from liver transplantation are increased in patients with coronary artery disease [39] or those with severe hypoxemia and elevated mean pulmonary artery pressure measurements [40,41]. However, the risk of poor outcomes does not appear to be increased in patients with mild to moderate pulmonary hypertension (pulmonary artery systolic pressure between 40 and 59 mmHg) [42]. (See "Liver transplantation in adults: Long-term management of transplant recipients", section on 'Cardiovascular risk' and "Management of cardiac risk for noncardiac surgery".)

Electrocardiogram — We obtain an electrocardiogram to look for signs of cardiac arrhythmias, conduction defects, signs of prior cardiac ischemia, or chamber enlargement/hypertrophy. (See "ECG tutorial: Basic principles of ECG analysis".)

Cardiac stress testing — To screen for coronary artery disease, we obtain noninvasive cardiac testing for all patients over 40 years of age and for those younger than 40 years if there are multiple risk factors for coronary artery disease. (See "Stress testing for the diagnosis of obstructive coronary heart disease".)

However, the ideal evaluation of coronary artery disease prior to liver transplantation continues to evolve:

- The American Heart Association and the American College of Cardiology Foundation has suggested noninvasive stress testing in liver transplantation candidates with no active cardiac conditions if there are multiple (three or more) risk factors for coronary artery disease present (eg, diabetes, prior cardiovascular disease, left ventricular hypertrophy, age greater than 60 years, smoking, hypertension, or dyslipidemia) [38]. In addition, the use of coronary computed tomography angiography (CCTA) is emerging for patients with known cardiac disease and those with abnormal screening tests. (See "Overview of established risk factors for cardiovascular disease", section on 'Established risk factors for atherosclerotic CVD'.)

- The American Association for the Study of Liver Diseases and the American Society of Transplantation has recommended noninvasive cardiac testing (either exercise stress

testing or pharmacologic stress testing) for all adults being evaluated for liver transplantation [1].

- Some cardiologists have recommended that patients with known coronary artery disease, diabetes mellitus, or more than two cardiovascular risk factors undergo coronary angiography to assess the extent and severity of coronary artery disease [43].

Another method that is being studied for pretransplant evaluation is submaximal cardiopulmonary exercise testing. One study found that the calculated anaerobic threshold (which corresponds with cardiorespiratory reserve) predicted post-transplantation mortality [44]. Survivors of liver transplantation had higher mean anaerobic thresholds than patients who did not survive (12.0 versus 8.4 mL/min/kg). This method of pretransplantation evaluation is not in widespread use. (See "Cardiopulmonary exercise testing in cardiovascular disease", section on 'Ventilatory anaerobic threshold determination'.)

If initial noninvasive testing is abnormal, cardiac catheterization is indicated. If clinically significant coronary artery stenoses are present, patients should be evaluated for revascularization prior to transplantation. (See "Percutaneous coronary intervention of specific coronary lesions" and "Left main coronary artery disease" and "Management of significant proximal left anterior descending coronary artery disease".)

Echocardiography — We obtain transthoracic echocardiography and bubble study to look for evidence of valvular heart disease, hepatopulmonary syndrome, portopulmonary hypertension, or decreased cardiac function, which may be a result of cirrhotic cardiomyopathy. (See "Definition and classification of the cardiomyopathies", section on 'Cirrhotic cardiomyopathy' and "Portopulmonary hypertension".)

Contrast-enhanced echocardiography is also part of the evaluation of patients with suspected hepatopulmonary syndrome. (See 'Pulse oximetry' below.)

Portopulmonary hypertension refers to pulmonary arterial hypertension that is associated with portal hypertension. Symptoms and signs of pulmonary hypertension (PH) may be difficult to recognize because they are nonspecific. Initially, patients present with fatigue, exertional dyspnea and a loud pulmonic component of the second heart sound. If the echocardiography suggests PH, additional testing is required to confirm the diagnosis and to rule out other causes of PH. (See "Portopulmonary hypertension", section on 'Diagnostic evaluation'.)

Pulse oximetry — Patients should undergo pulse oximetry to screen for hepatopulmonary syndrome. Hepatopulmonary syndrome is considered present when the following triad exists:

- Liver disease
- Impaired oxygenation
- Intrapulmonary vascular abnormalities, referred to as intrapulmonary vascular dilatations

The presence of hepatopulmonary syndrome worsens the prognosis of patients with cirrhosis. As a result, patients with hepatopulmonary syndrome receive standard Model for End-stage Liver Disease (MELD) exception points. If the oxygen saturation on pulse oximetry is low (<96 percent [45]), patients should have a blood gas obtained while breathing room air and undergo transthoracic contrast-enhanced echocardiography. Testing should also be obtained to rule out alternative causes for a low oxygen saturation. Testing to rule out other causes includes a chest radiograph, pulmonary function tests, and chest computed tomography (CT). (See "Hepatopulmonary syndrome in adults: Prevalence, causes, clinical manifestations, and diagnosis", section on 'Diagnostic evaluation' and "Model for End-stage Liver Disease (MELD)", section on 'Standard MELD exceptions in liver transplantation'.)

We also perform an arterial blood gas in patients with normal pulse oximetry to calculate their age-adjusted alveolar-arterial gradient (calculator 1).

Additional testing for pulmonary disease — The role of pulmonary function testing with diffusing capacity of the lungs for carbon monoxide to look for evidence of hepatopulmonary syndrome or primary lung disease is controversial, and there is wide variation in practice. Some transplantation centers perform such testing in all transplant candidates, while others restrict testing to patients with symptoms, smoking history, or prior known lung disease. Similarly, the use of chest radiography and chest CT scan to look for signs of pulmonary disease is variable. (See "Overview of pulmonary function testing in adults", section on 'Pulmonary function tests'.)

Cancer screening — Cancer screening should include abdominal CT scanning or magnetic resonance imaging (MRI) to look for hepatocellular carcinoma (HCC) and a skin examination to look for evidence of skin cancer. Colorectal cancer screening is indicated for patients who are ≥45 years of age (or younger for selected patients such as those with family history of colon cancer in a first-degree relative or those with primary sclerosing cholangitis). The approach to colon cancer screening is discussed separately. (See "Screening for colorectal cancer: Strategies in patients at average risk" and "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)

Screening for cervical cancer, breast cancer, and prostate cancer should be obtained when indicated based on the patient's sex and age. (See "Screening for cervical cancer in resource-rich settings" and "Screening for breast cancer: Strategies and recommendations" and "Screening for prostate cancer".)

Infectious disease evaluation and vaccinations — In addition to obtaining serologies for several viral infections, the infectious disease evaluation should include skin testing or interferon-gamma release assay for tuberculosis. If positive, treatment may be initiated prior to transplantation or deferred until after transplantation, depending on the clinical assessment of the patient (eg, treatment should be initiated prior to transplantation if the patient has any signs or symptoms of tuberculosis). Similarly, any required dental extractions should be carried out prior to transplantation. Patients from endemic areas should be screened for coccidiomycosis or strongyloides (table 4). (See "Infectious complications in liver transplantation".)

Several vaccinations are recommended prior to liver transplantation including COVID-19 [46], hepatitis A, hepatitis B, pneumococcus, influenza, diphtheria, pertussis, and tetanus. Immunizations in solid organ transplantation candidates are discussed in detail elsewhere. (See "Immunizations in solid organ transplant candidates and recipients".)

Hepatic imaging and HCC staging — Hepatic imaging should be obtained to assess the vasculature (to ensure there are no anatomic barriers to transplantation) and, in the case of HCC, for tumor staging. This is typically done with multiphase contrast-enhanced CT scanning or contrast-enhanced MRI. If cross-sectional imaging cannot be obtained, the hepatic vasculature can be assessed with transabdominal ultrasonography with Doppler imaging or contrast-enhanced ultrasonography (where available). (See "Staging and prognostic factors in hepatocellular carcinoma", section on 'Staging and prognostic scoring systems' and "Contrast-enhanced ultrasound for the evaluation of liver lesions", section on 'Liver transplantation'.)

Upper endoscopy — Upper endoscopy should be performed in patients with cirrhosis or portal hypertension to evaluate for varices. (See "Primary prevention of bleeding from esophageal varices in patients with cirrhosis", section on 'Screening for esophageal varices'.)

Bone density testing — Patients should be screened for osteoporosis with bone density testing. If osteoporosis is present, treatment should be initiated prior to transplantation. Oral bisphosphonates should be used with caution in patients with esophageal varices, and patients should be aware of the importance of taking the drugs as instructed (eg, sitting upright for at least 30 minutes after taking the drug). Patients who are osteopenic should receive calcium and vitamin D supplementation. (See "Overview of the management of osteoporosis in postmenopausal women", section on 'Choice of drug' and "Overview of the management of osteoporosis in postmenopausal women", section on 'Calcium/vitamin D'.)

Psychosocial evaluation and education — In addition to a standard medical evaluation, initial assessment should include an educational session discussing the risks and benefits of

transplantation, including the potential for poor outcomes. A psychological evaluation and assessment of the patient's social supports is another key part of the evaluation.

The purpose of this assessment is to identify issues that may impair a successful outcome after transplantation. These potential problems include a lack of insight into the nature of the transplantation procedure, post-transplantation care, and substance use disorders. The assessment includes education of the family and/or the patient's support network. The ability to comply with complex medical and behavioral regimens is crucial after any organ transplantation procedure. Recipients must be able to incorporate complicated medication regimens, follow-up appointments, and frequent laboratory visits into their lives. Making spouses, friends, and family aware of these requirements encourages patient compliance and may improve long-term success. (See "Screening for unhealthy use of alcohol and other drugs in primary care".)

In patients with a history of a substance use disorder (drugs or alcohol), treatment should be provided prior to transplantation in an effort to increase the likelihood of success after transplantation. The treatment requirements vary among different transplantation centers but often include participation in a structured rehabilitation and abstinence program, adequate social support to help maintain sobriety, and a minimum period of sobriety prior to listing for transplantation. (See "Liver transplantation for alcohol-associated liver disease".)

CANDIDATES FOR LIVING DONOR LIVER TRANSPLANTATION

Living donor liver transplantation (LDLT) in adults was initiated in response to the growing shortage of organs from deceased donors [47]. Recipients considered for LDLT should fulfill the same minimal listing criteria established for deceased donor liver transplantation. The goal is to avoid premature transplantation. The optimal Model for End-stage Liver Disease (MELD) score at which patients should undergo LDLT has yet to be determined [48]. The optimal MELD score is one that identifies the recipient when the chance of liver disease-related mortality is greater than the chance of mortality from surgical complications.

Evaluation of the adult living liver donor candidate, surgical technique, and outcomes of LDLT are discussed separately. (See "Living donor liver transplantation in adults".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Liver transplantation".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Liver transplant (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Indications for liver transplantation** – Indications for liver transplantation include acute liver failure, cirrhosis with complications, some liver neoplasms, and liver-based metabolic conditions with systemic manifestations. (See 'Indications' above.)

  - Patients with acute liver failure are given the highest priority for liver transplantation and should be referred to a liver transplantation center for evaluation as soon as possible. (See 'Acute liver failure' above.)

  - Patients with cirrhosis are typically candidates for liver transplantation once their biologic Model for End-stage Liver Disease (MELD) score is ≥15 (MELD-Na score). However, the transplantation evaluation is typically started once a patient has a MELD score >10. This permits the patient to meet the transplantation team prior to developing end-stage liver disease and ensures adequate time for the patient to complete the pretransplantation evaluation. (See 'Cirrhosis' above.)

    Patients with cirrhosis may also qualify for liver transplantation if they have a complication that qualifies for standard MELD exception points including hepatocellular carcinoma (HCC), hepatopulmonary syndrome, and portopulmonary

hypertension. (See "Model for End-stage Liver Disease (MELD)", section on 'Standard MELD exceptions in liver transplantation'.)

Finally, patients with cirrhosis may be considered for liver transplantation if they have other complications related to cirrhosis such as refractory ascites, though they do not receive standard MELD exception points. (See "Model for End-stage Liver Disease (MELD)", section on 'Petitioning for additional MELD points'.)

- Patients with some primary liver neoplasms (eg, HCC) may be candidates for liver transplantation, provided the neoplasms meet specific criteria. In addition, there may be a role for liver transplantation in patients with neuroendocrine tumors that have metastasized to the liver, but experience in this setting is limited. (See 'Liver neoplasms' above.)

- Liver-based metabolic conditions with systemic manifestations that may be treated with liver transplantation include familial amyloid polyneuropathy, primary hyperoxaluria, and cystic fibrosis. (See 'Metabolic disorders' above.)

- **Contraindications** – Contraindications to liver transplantation include cardiopulmonary disease that cannot be corrected and is a prohibitive risk for surgery, malignancy outside of the liver not meeting oncologic criteria for cure, metastatic HCC, persistent nonadherence with medical care, and lack of adequate social support. (See 'Contraindications' above.)

- **Pretransplantation evaluation** – The goal of the pretransplantation evaluation is to assess the patient's ability to tolerate the stress of surgery, immunosuppression, and the demands of post-transplantation care. Thus, each patient undergoes an extensive cardiopulmonary evaluation, screening for occult infection or cancer, and psychosocial evaluation (table 3). (See 'Pretransplantation evaluation' above.)

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Topic 4585 Version 36.0

GRAPHICS

Mnemonic for causes of acute liver failure: The ABCs

A	Acetaminophen, hepatitis A, autoimmune hepatitis, *Amanita phalloides* (mushroom poisoning), adenovirus
B	Hepatitis B, Budd-Chiari syndrome
C	Cryptogenic, hepatitis C, CMV
D	Hepatitis D, drugs and toxins
E	Hepatitis E, EBV
F	Fatty infiltration - acute fatty liver of pregnancy, Reye's syndrome
G	Genetic - Wilson disease
H	Hypoperfusion (ischemic hepatitis, SOS, sepsis), HELLP syndrome, HSV, heat stroke, hepatectomy, hemophagocytic lymphohistiocytosis
I	Infiltration by tumor

CMV: cytomegalovirus; EBV: Epstein-Barr virus; SOS: sinusoidal obstruction syndrome (veno-occlusive disease); HELLP: hemolysis, elevated liver enzymes, low platelets; HSV: herpes simplex virus.

Graphic 67925 Version 6.0

Child-Pugh classification of severity of cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time (seconds over control) or	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

INR: international normalized ratio.

Graphic 78401 Version 15.0

Pre-liver transplantation evaluation

Laboratory testing
ABO-Rh blood typing
Liver biochemical and function tests (ALT, AST, alkaline phosphatase, bilirubin, INR)
Sodium
CBC with differential
Creatinine clearance
Serum alpha-fetoprotein
Serum phosphatidyl ethanol (PEth)
Calcium and vitamin D levels
Serologies for CMV, EBV, varicella, HIV, HAV, HBV, HCV, RPR
Urinalysis
Urine drug screen
Cardiopulmonary evaluation
ECG
Cardiac stress test (exercise or pharmacologic) if over the age of 40 years or if there are multiple risk factors for coronary artery disease (followed by cardiac catheterization if positive)
Contrast-enhanced echocardiography
Pulse oximetry
Arterial blood gas
Chest radiography
Contrast-enhanced chest CT
Pulmonary function tests with DLCO
Cancer screening
Contrast-enhanced abdominal CT scan or MRI to look for hepatocellular carcinoma
Skin examination
Colonoscopy (if indicated based on patient's age or risk factors)
Cervical cancer screening and breast cancer screening for females (if indicated based on patient's age)
Prostate cancer screening for males (if indicated based on patient's age)
Infectious disease evaluation

Skin testing or interferon-gamma release assay for tuberculosis
Dental evaluation
Screening for coccidioidomycosis or strongyloides (for patients from endemic areas)
Psychosocial evaluation
Psychiatric evaluation
Social work evaluation
Patient education seminars
Evaluation for substance use disorders (drugs or alcohol)
Other testing
Bone density scan
Transabdominal ultrasound with Doppler imaging to assess the hepatic vasculature (if not already assessed with cross-sectional imaging)
Upper endoscopy in patients with cirrhosis or portal hypertension

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CBC: complete blood count; CMV: cytomegalovirus; CT: computed tomography; DLCO: diffusing capacity of the lungs for carbon monoxide; EBV: Epstein-Barr virus; ECG: electrocardiogram; HIV: human immunodeficiency virus; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; INR: international normalized ratio; MRI: magnetic resonance imaging; RPR: rapid plasma reagin.

Courtesy of Lorna Dove, MD, MPH and Robert Brown, MD, MPH.

Graphic 60683 Version 9.0

The pretransplant laboratory evaluation for solid organ transplant candidates

	Everyone	Vaccinate if seronegative or not vaccinated	With epidemiologic risk factors
Pathogen			
Cytomegalovirus	X		
Epstein Barr Virus	X		
Varicella	X	X	
HIV (HIV-1 and -2 immunoassay)*	X		
Hepatitis B virus (HBsAg, HBsAb, HBcAb)*¶	X	X	
Hepatitis C virus*¶	X		
Treponema pallidum (Venereal Disease Research Laboratory or rapid plasma reagin)	X		
Tuberculosis (screening skin test or interferon-gamma release assay for tuberculosis$^{\Delta}$)	X		
Mumps, measles, and rubella	X	X	
Toxoplasma gondii (heart transplant candidates)	X		
Coccidioides antibody			X
Histoplasma antibody			X
Blastomyces antibody			X
Strongyloides stercoralis serology$^{\diamond}$			X
Trypanosoma cruzi (Chagas disease)			X
Leishmania spp (visceral disease only, may cross react with *T. cruzi*)			X
Schistosoma spp (cystoscopy may be useful in renal transplant candidates)			X
HTLV1 and 2 (suboptimal screening platforms in low-prevalence areas)			X
Hepatitis A serology		X	X
SARS-CoV-2 (COVID-19) NAAT§		X	

Other tests			
Chest radiograph, urinalysis	X		
Stool exam for ova and parasites			X

Refer to UpToDate content for detail on vaccination schedules and treatment of infections identified during screening.

HBsAg: hepatitis B surface antigen; HBsAb: hepatitis B surface antibody; HBcAb: hepatitis B core antibody; HTLV: human T-lymphotropic virus; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease 2019; NAAT: nucleic acid amplification testing.

* Repeat as close as possible to time of transplant (at least within one week of transplant) and repeat for recipients of organs from donors with increased risk for transmission of infection. Refer to the UpToDate topic on screening and diagnostic testing for HIV infection for the preferred approach.

¶ For individuals with known infection or at increased risk for infection (based on risk factors detected in the medical and/or social history), quantitative nucleic acid testing should also be performed.

Δ Refer to the UpToDate topic on tuberculosis in solid organ transplant candidates for the preferred approach.

◇ Strongyloides stercoralis: Empiric therapy (ivermectin × 2 doses) is often used in place of serologic testing for appropriate epidemiologic history.

§ All transplant candidates should be screened for SARS-CoV-2 (sensitive nucleic acid assay) during pandemic and deferred if positive and if feasible. Transplant candidates with ongoing respiratory illness or radiographic pulmonary infiltrates should generally be deferred. SARS-CoV-2 antibody screening assays are highly variable and probably not useful for routine screening; may be useful in demonstrating immune response to prior infection.

Graphic 59792 Version 16.0

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