



Complete Summary

GUIDELINE TITLE

Liver transplantation.

BIBLIOGRAPHIC SOURCE(S)

Carithers RL Jr. Liver transplantation. American Association for the Study of Liver Diseases. Liver Transpl 2000 Jan;6(1):122-35. [141 references] [PubMed](#)

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

1. Chronic liver failure from:
 - a. cholestatic disorders (e.g., primary biliary cirrhosis, sclerosing cholangitis, and extrahepatic biliary atresia);
 - b. chronic hepatitis (e.g., hepatitis B, hepatitis C, and autoimmune hepatitis);
 - c. alcoholic liver disease;
 - d. metabolic diseases (e.g., Wilson's disease, hereditary tyrosinemia type I, hereditary hemochromatosis, alpha₁-antitrypsin deficiency, nonalcoholic steatohepatitis); and
 - e. cirrhosis of unknown cause (cryptogenic cirrhosis);
2. Acute liver failure (fulminant hepatic failure [FHF]) of any cause;
3. Hepatocellular carcinoma (HCC); and
4. Other end-stage liver disease

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Gastroenterology
Infectious Diseases
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide a data-supported approach to the treatment of patients considered for liver transplantation

TARGET POPULATION

Individuals with acute or chronic liver failure

INTERVENTIONS AND PRACTICES CONSIDERED

Liver transplantation, including

1. Selection of patients for liver transplantation
2. Timing of transplantation

MAJOR OUTCOMES CONSIDERED

Outcome of transplantation versus the natural history of the disease in question with respect to:

- Survival rates
- Morbidity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A formal review and analysis of the recent published world literature on liver transplantation (Medline search from 1990 to 1998) was conducted.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

In an attempt to standardize recommendations, the Practice Guidelines Committee of the American Association for the Study of Liver Diseases modified the categories of the Quality Standards of the Infectious Diseases Society of America:

Grade I: Evidence from multiple well-designed, randomized controlled trials, each involving a number of participants to be of sufficient statistical power.

Grade II: Evidence from at least one large, well-designed clinical trial with or without randomization, from cohort or case-control analytic studies or well-designed meta-analysis.

Grade III: Evidence based on clinical experience, descriptive studies, or reports of expert committees.

Grade IV: Not rated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

These guidelines were commissioned and approved by the American Association for the Study of Liver Diseases (AASLD). In cooperation with the AASLD Practice Guidelines Committee, the guidelines were written by Robert L. Carrithers, Jr., MD. The editors of the journal *Liver Transplantation* have published the guidelines as a courtesy to AASLD and for informational purposes for its readers; the guidelines have not been peer-reviewed through the journal's process.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations are followed by quality of evidence ratings (Grades I-IV) and categories reflecting the evidence to support the use of a recommendation (A-E), which are defined at the end of the "Major Recommendations" field.

Cholestatic disorders

Liver transplantation is indicated for appropriately selected patients with advanced primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC) (rating, II A, III CD).

Childhood cholestatic disorders

Liver transplantation is indicated in appropriately selected children with extrahepatic biliary atresia if the diagnosis is delayed beyond 3 months after birth, portoenterostomy is unsuccessful, or intractable portal hypertension or liver failure develop despite a successful Kasai procedure (rating, III AC).

Chronic hepatitis

Liver transplantation is indicated for appropriately selected patients with decompensated cirrhosis secondary to chronic hepatitis C, hepatitis B, or autoimmune hepatitis. Patients undergoing transplantation for hepatitis B need specialized management to prevent severe recurrent disease after transplantation (rating, III ACD).

Alcoholic liver disease

Selected patients with alcoholic liver disease are candidates for liver transplantation. To be considered for transplantation, potential candidates should have careful assessment by a health care professional experienced in the management of patients with addictive behavior (rating, III ACD).

Hereditary hemochromatosis

Liver transplantation is indicated for carefully selected patients with hereditary hemochromatosis. However, because the results have been disappointing, more research is needed to determine the optimum use of transplantation in these patients (rating, III D).

Alpha₁-antitrypsin deficiency

Selected patients with severe liver disease secondary to alpha₁-antitrypsin deficiency should be considered for liver transplantation (rating, III ACD).

Wilson's disease

Liver transplantation is indicated in selected patients with Wilson's disease who present with fulminant hepatic failure (FHF) and in those with chronic liver disease who fail to respond to chelation therapy or who relapse after discontinuing therapy (rating, III ACD).

Hepatobiliary malignancies

Liver transplantation can be very effective treatment for patients with cirrhosis in whom hepatocellular carcinoma (HCC) is confined to the liver. The best candidates for transplantation are those with single tumors less than 5 cm in size or multiple tumors, each less than 3 cm in size. Patients with radiologic evidence of vascular invasion or metastatic disease are not candidates for transplantation. Because of the extraordinary risk for hepatocellular carcinoma, children with tyrosinemia should be considered for transplantation at an early age. Patients with cholangiocarcinoma or metastatic tumors (excluding neuroendocrine tumors) should not undergo liver transplantation except in carefully controlled trials (rating, III AC).

Fulminant hepatic failure

Patients with suspected FHF should be referred to a transplant center as quickly as possible. Patients with FHF with progressive encephalopathy and coagulopathy should receive the highest priority for liver transplantation (rating, III ACD).

Selection of patients for transplantation

Patients should only be considered for transplantation if they have a reasonable chance of surviving the perioperative period. Those selected must be able to comply with long-term medication therapy and refrain from addictive forms of behavior. They should have no other major medical illness significantly curtailing life expectancy (rating, III ACE).

Prognosis-based timing of transplantation

Patients with cirrhosis should be referred for transplantation when they develop evidence of synthetic dysfunction, experience their first major complication (ascites, variceal bleeding, or hepatic encephalopathy), or develop malnutrition. Children with chronic liver disease should be referred when they fall off their growth curves. If patients with cirrhosis and hepatocellular malignancies are to be considered for transplantation, they should be referred as soon as the tumor is recognized. Patients with potential FHF should be referred as soon as a persistently prolonged prothrombin time is identified or at the first sign of hepatic encephalopathy (rating, III ACE).

Adult patients with cirrhosis should be listed for transplantation once the Child-Turcotte-Pugh (CTP) score is 7 or greater. Patients with FHF should be listed if the pH is less than 7.3 (acetaminophen toxicity) or if grade 2 hepatic encephalopathy develops (rating, III AC).

Definitions:

Quality of evidence

Grade I: Evidence from multiple well-designed, randomized controlled trials, each involving a number of participants to be of sufficient statistical power.

Grade II: Evidence from at least one large, well-designed clinical trial with or without randomization from cohort or case-control analytic studies or well-designed meta-analysis.

Grade III: Evidence based on clinical experience, descriptive studies, or reports of expert committees.

Grade IV: Not rated

Evidence to support use

A: Survival benefit

B: Improved diagnosis

C: Improvement in quality of life

D: Relevant pathophysiologic parameters improved

E: Impacts cost of health care

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is specifically stated for each recommendation (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Extended survival with excellent quality of life after transplantation in patients with end-stage liver disease
- Appropriate use of scarce donor organs through careful patient selection for transplantation
- Optimal timing of surgery

Subgroups Most Likely to Benefit:

Historic experience suggests that the best hepatocellular carcinoma (HCC) candidates for transplantation are those with a single lesion less than 5 cm in diameter or, if more than one lesion is present, no lesion greater than 3 cm in diameter. However, patients with large epitheliomas or fibrolamellar hepatomas usually do well.

POTENTIAL HARMS

- Rejection, graft failure, and need for retransplantation
- Although not well characterized, suboptimal results, in patients with liver transplantation from hemochromatosis, appear to result from a high rate of postoperative infection and occasional deaths from cardiomyopathy.

Subgroups Most Likely to be Harmed:

There is an increased blood loss, longer surgical time, and increased perioperative complications of transplantation in children with a previous portoenterostomy.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to transplantation:

- There are few absolute medical or surgical contraindications to liver transplantation. There is no specific age limitation to successful transplantation. Patients must have adequate cardiac and pulmonary function to tolerate major surgery. Patients with cirrhosis can develop significant hypoxia or pulmonary hypertension. Moderate abnormalities of gas exchange or pulmonary pressures are not a deterrent to successful transplantation. However, patients with severe hypoxia or right atrial pressure greater than 60 mm Hg rarely survive surgery and the perioperative recovery period. Uncontrolled systemic infection is an obvious contraindication to high-dose immunosuppressive therapy. In addition, the prognosis of other serious medical conditions should be reasonable if transplantation is to be contemplated. Patients with extrahepatic malignancies other than squamous cell skin carcinoma should be deferred for at least 2 years after completion of curative therapy before transplantation is attempted. Finally, significant psychiatric or neurological disorders must be under excellent medical control with assurance that the patient can be compliant after transplantation.
- Absence of a viable splanchnic venous inflow system is the most commonly encountered surgical contraindication to liver transplantation. Thrombosis of the main portal vein can be successfully bypassed; however, if the entire

portal venous system is occluded, attempts at transplantation have rarely been successful. The final and most frequently encountered contraindication to transplantation is ongoing destructive behavior caused by drug and alcohol addiction. Medical compliance should be effectively addressed before patients are considered for transplantation.

QUALIFYING STATEMENTS

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- These guidelines are intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in almost every case.
- Because of logistic restraints, no randomized trials have been performed to prove the efficacy of liver transplantation. However, various registries provide a wealth of information concerning the outcome of liver transplantation for various conditions. These guidelines have been developed to reflect a consensus from the literature and outcomes data comparing transplant results with the natural history of selected disease states, as well as the views of most experts involved in liver transplantation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Jan

GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization

SOURCE(S) OF FUNDING

American Association for the Study of Liver Diseases

GUIDELINE COMMITTEE

Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Robert L. Carrithers, Jr., MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The guideline is being revised by the American Association for the Study of Liver Diseases.

GUIDELINE AVAILABILITY

Electronic copies: Available in portable Document Format (PDF) from the [American Association for the Study of Liver Diseases Web site](#).

Print copies: Available from the American Association for the Study of Liver Diseases, 1729 King Street, Suite 200; Alexandria, VA 22314; Phone: 703-299-9766; Web site: www.aasld.org; e-mail: aasld@aasld.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 9, 2003. The information was verified by the guideline developer as of June 12, 2003.

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