

Criteria and Indications for Liver Transplantation: An Integrative Review

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ABSTRACT

Introduction: Liver transplantation is essential to treat terminal liver diseases or those that compromise quality of life. **Objectives:** This study reviews the indications for liver transplantation, such as cirrhosis, cholangitis, Budd–Chiari syndrome, fulminant liver failure, and hepatocellular carcinoma. **Methods:** The integrative review was carried out by searching the SciELO, Virtual Health Library, and Google Scholar databases, selecting thirteen studies after analyzing the criteria defined by the authors. **Results:** Thirteen studies on liver transplantation were analyzed, highlighting cirrhosis (33.3%), hepatocellular carcinoma (38.0%), and acute liver failure (5.8%), with good results in acute failure and initial tumors. **Conclusion:** The indication for transplantation should follow strict criteria, especially hepatocellular carcinoma, alcoholic cirrhosis, and cirrhosis caused by the C virus.

Descriptors: Liver transplantation; Hepatopathies; Liver failure.

Crítérios e Indicações para o Transplante Hepático: Uma Revisão Integrativa

RESUMO

Introdução: O transplante hepático é essencial para tratar doenças hepáticas terminais ou que comprometem a qualidade de vida. **Objetivos:** Este estudo revisa as indicações para o transplante de fígado, como cirrose, colangite, síndrome de Budd–Chiari, insuficiência hepática fulminante e carcinoma hepatocelular. **Métodos:** A revisão integrativa foi realizada com buscas nas bases SciELO, Biblioteca Virtual de Saúde e Google Acadêmico, selecionando treze estudos após análise dos critérios definidos pelas autoras. **Resultados:** Foram analisados treze estudos sobre transplante hepático, destacando cirrose (33,3%), carcinoma hepatocelular (38,0%) e insuficiência hepática aguda (5,8%), com bons resultados em insuficiência aguda e tumores iniciais. **Conclusão:** A indicação para o transplante deve seguir critérios rigorosos, destacando carcinoma hepatocelular, cirrose alcoólica e cirrose pelo vírus C.

Descritores: Transplante hepático; Hepatopatias; Falência hepática.

INTRODUCTION

The liver is the largest gland in the body and plays an essential role in the metabolism of glucose and lipids, as well as converting ammonia into urea. It is also responsible for protein synthesis, fat metabolism, vitamin storage, and bile production.

In Brazil, the first liver transplants occurred in 1968, at the Hospital das Clínicas of the Universidade de São Paulo (USP). In 1984, liver transplantation was recognized as a medical therapy and ceased to be an experimental procedure¹. According to the Brazilian Transplant Association, Brazil is the second country in the world in terms of the number of transplants carried out annually, with 2,365 liver transplants carried out in 2023, more than 90% of which were performed by the Unified Health System.²

Orthotopic liver transplantation is the treatment indicated for severe liver diseases that are incurable by other methods, replacing the diseased liver with a healthy one from a living or deceased donor. It is recommended for terminal cases with high mortality in conventional treatments, offering greater survival and quality of life. It can be elective or urgent, with most elective cases involving severe cirrhosis and low survival expectancy.

Therefore, the objective of this study is to review the main conditions and diseases that may lead to an indication for liver transplantation.

METHODOLOGY

The method selected was an integrative review (IR). The work involved formulating a guiding question, searching the literature for primary studies, evaluating the studies included in the review, analyzing, and synthesizing the results and presenting the IR.

The IR's guiding question arose from the need to understand how various liver diseases influence the decision to undergo a liver transplant. This resulted in the following question: "What are the main liver diseases that indicate the need for liver transplantation?"

In the bibliographic survey, a search was carried out in the SciELO, Virtual Health Library, and Google Scholar databases, as well as in chapter 18, "Liver and Biliary Tract," in the book *Robbins & Cotran Pathologic Basis of Disease*³. The following descriptors were used to search for articles in the literature: "*transplante hepático*," "*hepatopatias*," and "*falência hepática*" (Table 1).

Table 1. Articles included in this study.

Databases	Included studies
SciELO "Falência Hepática"	8 articles included
Biblioteca Virtual de Saúde "Hepatopatias"	1 article included
Google Acadêmico "Transplante Hepático"	4 articles included
<i>Robbins & Cotran Pathologic Basis of Disease</i>	Chapter 18 – "Liver and Biliary Tract"

Source: Elaborated by the authors.

The inclusion criteria for selecting the analyses were based on full-text articles published in Portuguese on the subject of IR, as well as texts published and indexed in these databases, with a publication date limitation of the last 25 years. The exclusion criteria covered articles that did not comply with the defined scope, those published after the established date, and studies with insufficient data.

The initial selection was conducted by reading the titles and abstracts. The articles were then fully analyzed and those that met the inclusion criteria were incorporated into the IR sample (Table 2).

Table 2. Identification, selection, and inclusion of studies in the IR.

Identification	Screening	Included
SciELO (n = 51)	Exclusion after reading title and abstract (n = 42)	Final selection (n = 8)
Virtual Health Library (n = 74)	Exclusion after reading title and abstract (n = 73)	Final selection (n = 1)
Google Scholar (n = 25)	Exclusion after reading title and abstract (n = 21)	Final selection (n = 4)

Source: Elaborated by the authors.

RESULTS

The indication for liver transplantation is for patients with advanced liver disease, whose life expectancy is less than 20% in 12 months without the procedure. The assessment requires a detailed understanding of the history of the disease and prognostic factors, considering clinical and biochemical parameters. Asymptomatic patients may not be ready for transplantation, while those with significant symptoms that affect their quality of life may opt for the procedure, even with a favorable life expectancy.⁴

Table 3 summarizes the studies analyzed, highlighting the main findings regarding liver transplant patients. A total of 85 medical records were assessed, 52 of which were transplant recipients, with a post-transplant death rate of 38% and only 1% mortality on the waiting list, demonstrating the effectiveness of MELD in prioritizing transplants¹. Alcoholic cirrhosis

was the main indication (31.4%), and hypertension the most common comorbidity (51.4%). The average age was 52.7 years, with a male predominance (60.8%). In addition, complications such as ascites (56.9%) and portal hypertension (52.9%) were frequent⁸. The King's College criteria, which are widely used, have good specificity but low sensitivity. Although various markers have been tested to improve prognostic accuracy, the results are still inconclusive. Factors such as age, ABO incompatibility, and poor graft quality have been identified as possible causes of therapeutic futility. Furthermore, extracorporeal liver support systems have shown clinical and laboratory improvements, but without a significant impact on patient survival.⁹

Table 3. Summary of primary studies according to authors, objective, method, and main results.

Authors	Title	Objectives	Results
Vieira et al. ⁵	<i>Sucesso do transplante hepático de acordo com o tempo em lista</i>	To evaluate the correlation between time on the waiting list and the pre-transplant MELD value with the prognosis of patients after liver transplant surgery.	A total of 85 medical records were analyzed, 52 of which were of transplant patients. Of these, 32 died post-transplant and one before the procedure. Another 40 medical records were illegible or unavailable. The MELD in the listing ranged from 8 to 40, predominantly between 13 and 20. The study showed the effectiveness of MELD in selecting patients, with low mortality (1%) on the waiting list and a post-transplant death rate of 38%, reinforcing its usefulness in prioritizing transplants.
Ferreira ⁶	<i>Indicações e contra-indicações para o transplante hepático: saber para cuidar</i>	Clarifying the criteria for inclusion in the liver transplant program, analyzing the impact of liver disease on patients' quality of life, as well as emphasizing the importance of organ donation for transplants.	Liver transplantation is recommended by specialists following established protocols to extend the patient's life and ensure quality of care. The decision considers the progression of the disease, prognostic factors, and the ineffectiveness of other treatments. Candidates usually have liver damage, multiple hospitalizations, and various challenges.
Grupo Integrado de Transplante de Fígado ⁷	<i>Protocolo de transplante hepático</i>	The purpose of this protocol is to guide professionals in the management of patients referred to the Liver Transplant Service at HC-FMRP-USP, covering clinical conduct from admission to the late postoperative period.	The assessment of patients with liver disease begins with the hepatologist, who determines the need for a transplant. If deemed eligible, the patient undergoes evaluations by the surgical team, nursing staff, social workers, and psychologists. Inclusion on the waiting list takes place after joint analysis. The authors outline clinical procedures from patient admission to the late postoperative period.
Gomes ⁸	<i>O desempenho dos estados do Nordeste na realização do transplante hepático: 2015 a 2019</i>	To compare the performance of the states in the Northeast region in terms of liver transplant procedures between 2015 and 2019.	The state of Ceará stands out with a high rate of liver transplants per million inhabitants in the Northeast region, followed by Pernambuco. Bahia, Maranhão, and Paraíba have low rates of liver transplants per million inhabitants. The states of Alagoas, Piauí, Rio Grande do Norte, and Sergipe do not perform liver transplantation due to the absence of specialized centers in their territories.
Castro e Silva Jr. ⁴	<i>Transplante de fígado: indicação e sobrevida</i>	To describe the main indications for liver transplantation and its clinical and biochemical parameters, as well as the contraindications for the procedure.	The authors detail the liver diseases with the most frequent indications, especially cirrhosis, fulminant hepatic failure and hepatocarcinoma.
Pacheco ¹	<i>Transplante de fígado no Brasil</i>	To describe the current situation of liver transplantation in Brazil and to explore future questions about improvements in the donation-transplantation process.	A great development in liver transplantation has been observed in Brazil, marked by an increase in both transplant centers and procedures performed.
Aguiar et al. ⁹	<i>Gravidade da doença hepática e qualidade de vida no transplante de fígado</i>	To analyze the influence of the severity of liver disease on the quality of life of patients before and after liver transplantation.	Before transplantation, Child C patients had lower quality of life scores than Child A patients. Patients with a MELD less than or equal to 15 had a significant increase in the means in 10 domains, while patients with a MELD greater than 15 had an increase in 12 domains.

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Table 3. Continuation...

Authors	Title	Objectives	Results
Siqueira et al. ¹⁰	<i>Perfil epidemiológico e complicações de pacientes em fila de espera para transplante de fígado</i>	To identify the epidemiological profile of liver transplant candidates and the complications that occurred up to the sixth month after joining the waiting list.	The average age of the participants was 52.7 years, predominantly men (60.8%) with a low level of education. Hypertension was the most common comorbidity (51.4%) and alcoholic cirrhosis the main indication for transplantation (31.4%). The majority were overweight (BMI 28.8 kg/m ²) and had blood type O (58.8%). The average MELD on the waiting list was 17.9, with a predominance of Child–Pugh class B. The most frequent complications were ascites (56.9%) and portal hypertension (52.9%). In the end, 56.9% were awaiting a transplant, 19.6% were transplanted, and 23.5% died.
Dias et al. ¹¹	<i>CrITÉRIOS de Seleção para Transplantação hepática e modalidades terapêuticas como ponte na falência hepática aguda</i>	To analyze selection criteria for transplantation in acute liver failure, focusing on new markers; to identify poor prognostic factors; and to evaluate the impact of extracorporeal liver support systems on patient survival.	The King's College criteria are widely used but have low sensitivity despite good specificity. Although various markers have been tested to improve prognostic accuracy, the results are still unclear. Factors such as age, ABO incompatibility, and poor graft quality are indicated as potential causes of therapeutic futility. Extracorporeal liver support systems improve clinical and laboratory parameters but do not show a significant increase in patient survival.
Meirelles Júnior et al. ¹²	<i>Transplante de fígado: história, resultados e perspectivas</i>	The purpose of this article was to briefly review the history and present recent results of liver transplantation in Brazil and worldwide, as well as to discuss controversial topics and perspectives.	Liver transplantation began in 1963, with important advances such as the use of cyclosporine (1979) and tacrolimus (1990). At Hospital Israelita Albert Einstein, it began in 1990, with more than 1,400 performed to date. In 2013, 102 transplants were carried out, with a survival rate of 82.4% in the first year. The biggest challenge is the lack of donors, and it is crucial to improve the selection and preservation of organs to meet the growing demand.
Marroni et al. ¹³	<i>Transplante hepático em adultos</i>	To describe the logistical process involved from liver procurement to liver transplantation.	Technical and immunological advances and greater experience have changed the approach to transplants, allowing for earlier indications. This improved the recipients' condition and increased survival by 30–40% in one year.
Ferreira et al. ¹⁴	<i>Transplante Hepático</i>	To review the clinical aspects and theoretical bases of pediatric liver transplantation, focusing on the pre- and postoperative periods.	Clinical aspects of the preoperative phase were reviewed, covering the indications, contraindications, and assessments that the patient should undergo, as well as aspects of the postoperative period, with its stages: early (first week), after the first week, and in the long term, mainly discussing complications and the treatment of each one.
Furlan et al. ¹⁵	<i>Transplante de fígado com órgãos de critérios expandidos e complicações relacionadas à internação</i>	The aim of this study was to evaluate the use of expanded criteria in organ donation in liver transplants and to analyze the relationship between the number of these criteria in the same donor, as well as the recipient's outcomes during hospitalization.	A total of 37 liver transplants were carried out. The recipients had an average MELD-Na of 21.5. Only 1 patient received a donor graft without any expanded criteria. The other donors had between 1 and 5 expanded criteria for liver donation on their donation form. In conclusion, no significant difference was found between the variables assessed in patients who received organs with more criteria. The use of expanded criteria organs, as well as the number of criteria in the same organ, does not alter the parameters studied in this research.

Source: Elaborated by the authors.

Candidates waiting for a liver transplant are considered to meet four fundamental requirements:

- Establishment of a specific diagnosis of the disease;
- Clear evidence of the severity of the illness through documented proof;
- Identification of possible complications that could compromise the patient's survival;
- Estimated patient survival with and without transplantation.

Organ allocation criteria follow global guidelines, prioritizing emergency situations such as fulminant hepatitis and postoperative thrombosis. The Model for End-stage Liver Disease (MELD) system has been used in Brazil since 2007 to assess the severity of transplant candidates, assigning an index from 6 to 40. Patients with a higher MELD, indicating greater severity and lower survival expectancy, have priority on the liver transplant waiting list.

LIVER DISEASES WITH REGULAR INDICATIONS

Primary biliary cirrhosis

Primary biliary cirrhosis (PBC) is an inflammatory autoimmune disease that mainly affects the intrahepatic bile ducts, causing their nonsuppurative destruction. This condition can progress to periportal hepatitis, cirrhosis, and other

complications. It is characterized by the destruction of medium-sized bile ducts and poses a serious threat to liver health.^{4,7}

Primary biliary cirrhosis mainly affects middle-aged women, with an insidious onset and symptoms such as fatigue, itching, abdominal discomfort, and hepatomegaly. Indications for transplantation include situations such as progressive jaundice, bleeding esophageal varices, uncontrollable ascites, or hepatic encephalopathy. The prognosis for PBC after transplantation is good, with a five-year survival rate of 90%, and transplantation is the most effective treatment for terminal stages of the disease.^{4,7}

Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is an idiopathic disease characterized by inflammation and obliterative fibrosis of the intrahepatic and extrahepatic bile ducts with dilatation of the preserved segments. It is often associated with inflammatory bowel disease, especially chronic ulcerative colitis.^{4,7}

Primary sclerosing cholangitis mainly affects adult men aged between 20 and 40, who are good candidates for liver transplantation. The clinical indications are similar to those for PBC, with a survival rate after transplant of 85% at 1 year and 75% at 3 years.^{4,7}

Liver cirrhosis

The main causes of cirrhosis include alcohol abuse, viral hepatitis, and nonalcoholic steatohepatitis. Other causes are biliary diseases and iron overload. Around 40% of patients with cirrhosis are asymptomatic until the advanced stages. When patients present symptoms, they are usually nonspecific, such as anorexia, weight loss, and weakness, and in advanced stages they can include signs of liver failure.^{4,7}

Liver cirrhosis is the main indication for liver transplantation, accounting for 70% to 90% of cases, the main causes include alcohol consumption and viral hepatitis, particularly hepatitis B and C, which can lead to cirrhosis in 20% to 50% of instances. Recurrence of viral hepatitis in the transplanted liver is common, with recurrence of B virus being more severe than that of C virus. The survival rate for patients transplanted due to cirrhosis is around 60% over 5 years.^{4,7}

Budd–Chiari syndrome

Budd–Chiari syndrome is a rare hepatic venous disease, more common in young adults, which can manifest in an acute, subacute, or chronic form, resulting in portal hypertension. Liver transplantation is indicated when ascites cannot be controlled, or liver failure occurs. An angiographic evaluation is necessary to assess significant thrombotic involvement and the chronicity of the clinical picture, evidenced by the presence of ascites, digestive hemorrhage, or hepatic encephalopathy.^{4,7}

Alcoholism

Alcoholism affects various systems in the body, and alcoholic cirrhosis is one of the main causes of transplantation, especially in men. To increase the chances of success, transplant candidates must be abstinent for at least 6 months. Recurrence of alcohol use is more common in those who have stopped drinking for less than 6 months. The 5-year results of the transplant are similar to those of patients with other liver diseases, with a relapse rate of less than 15%.^{4,7}

Fulminant liver failure

Liver failure is the most serious consequence of liver disease, resulting in massive hepatic necrosis and encephalopathy, with a mortality rate of around 80%. Referral to a transplant center should occur when the first signs of hepatic encephalopathy appear. Transplantation is indicated when coagulation factors, such as factor V, are below 20%, associated with a state of coma or severe mental confusion, with a mortality rate of over 90%.^{4,7}

Liver tumor

Primary malignant liver tumors have a primary indication for liver transplantation, especially when it is a single tumor with a diameter of up to 5 cm or up to three 3 cm lesions, without vascular invasion or metastasis. Transplantation is the only treatment that guarantees the complete removal of all hepatic tumor foci, as well as tissue at risk of tumor recurrence, resulting in significantly higher tumor recurrence-free survival rates than those obtained by surgical resection.^{4,7}

Hepatocarcinoma is a common complication in cirrhotic patients with a 5-year survival rate of 18% to 35%, which is considered unacceptable for transplantation.^{4,7}

Unusual indications

With the exception of chronic rejection, the indications for retransplantation are urgent: hyperacute rejection, lack of immediate graft function, and hepatic artery thrombosis, as long as they occur within the first thirty days after liver transplantation.^{4,7}

CONCLUSION

Liver transplantation is essential for patients with advanced liver disease and conditions that do not respond to other therapies. This study highlighted that cirrhosis, acute liver failure, metabolic diseases, hepatocellular carcinoma, and congenital diseases are the main indications for transplantation, providing a significant improvement in quality of life and patient survival. With the advancement of transplant techniques and the broadening of eligibility criteria, it is becoming increasingly important to carry out a careful evaluation to ensure that the transplant is targeted at cases where its benefit is maximum, promoting positive and sustainable results for patients.

CONFLICT OF INTEREST

There is no conflict of interest.

AUTHOR'S CONTRIBUTION

Substantial scientific and intellectual contributions to the study: Araújo YCR, Nascimento MML; **Conception and design:** Araújo YCR; **Data analysis and interpretation:** Araújo YCR; **Article writing:** Araújo YCR; **Critical review:** Araújo YCR, Nascimento MML; **Final approval:** Nascimento MML.

DATA AVAILABILITY STATEMENT

All the data was generated/analyzed in this article.

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