Evaluation and Prognosis of Persons with Cirrhosis

This is a PDF version of the following document:
Module 2: Evaluation, Staging, and Monitoring of Chronic Hepatitis C
Lesson 5: Evaluation and Prognosis of Persons with Cirrhosis

You can always find the most up-to-date version of this document at https://www.hepatitisC.uw.edu/go/evaluation-staging-monitoring/evaluation-prognosis-cirrhosis/core-concept/all.

Background

Overview

In an estimated 20 to 30% of persons with hepatitis C virus (HCV) infection, persistent liver inflammation leads to fibrosis and eventual development of cirrhosis.[1,2,3] Advanced fibrosis and cirrhosis—at their early stages—are not usually clinically apparent or symptomatic.[4] As individuals develop more extensive hepatic fibrosis, physiologic complications can develop, such as increased pressure within the portal system, disruption in bilirubin metabolism, and reduced production of coagulation factors and other proteins.[5,6] This lesson discusses the clinical considerations that come with the care of a person with HCV-related cirrhosis.

Defining Compensated and Decompensated Cirrhosis

Once it has been established that an individual has cirrhosis, it is very important to determine whether they have compensated or decompensated cirrhosis.[7] Persons with compensated cirrhosis often do not have signs or symptoms related to their cirrhosis, although they may have evidence of portal hypertension, such as esophageal or gastric varices.[8,9,10] In contrast, persons with decompensated cirrhosis often have symptomatic complications related to cirrhosis, including those related to hepatic insufficiency (jaundice or hepatic encephalopathy) and those related to portal hypertension (ascites or variceal hemorrhage).[11] Some experts have proposed a 4-stage cirrhosis classification system to risk-stratify individuals according to the presence of ascites, esophageal varices, and variceal bleeding to differentiate and stage compensated and decompensated disease, although the Child-Turcotte-Pugh score (discussed later in this lesson) is more widely used (Figure 1).[12,13]

Importance of Distinguishing Compensated versus Decompensated Cirrhosis

Prognosis and survival are markedly better in persons with compensated cirrhosis than in those with decompensated cirrhosis (Figure 2).[14,15] In addition, the presence of decompensated cirrhosis can have major implications regarding management and prevention of cirrhosis-related complications, as well as the potential need for a referral for liver transplantation evaluation.[16] In general, any person with decompensated cirrhosis should receive evaluation and medical care from a hepatologist or liver diseases specialist.[7]

Evaluation of Persons with Cirrhosis

Once an individual is diagnosed with cirrhosis, there are key elements of the history, physical examination, and laboratory studies that need to be addressed and monitored.

Medical History

- **Alcohol Use:** Detailed quantitative information should be obtained from the patient regarding current and past alcohol use. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) offers resources for clinicians on how to take an appropriate alcohol history (NIAAA Screen and Assess) and how to conduct a brief intervention (NIAAA Conduct a Brief Intervention). Excessive alcohol use (greater than 40 grams per day in women and greater than 60 grams per day in men) in patients with chronic HCV infection has been associated with accelerated fibrosis progression.[17] In addition, for those individuals with chronic HCV and more advanced liver disease, ongoing alcohol use will impact their eligibility for liver transplantation.
- **Injection Drug Use**: Recent or active injection drug use should be addressed through the application of harm reduction principles. A person with chronic HCV and cirrhosis who continues to use injection drugs remains at risk for acquiring other bloodborne viruses, such as HIV and hepatitis B virus (HBV), and they can become reinfected with HCV after obtaining a sustained virologic response with treatment. For persons with decompensated cirrhosis, ongoing illicit drug use may impact consideration for liver transplantation.
- **Medication Use**: For individuals with cirrhosis, medication use, including all nonprescription drugs and prescription drugs, should be carefully reviewed. Persons with cirrhosis should be counseled to limit potentially hepatotoxic drugs. LiverTox, a comprehensive database developed by the National Institutes of Health (NIH), is an excellent online resource for clinicians to query the potential hepatotoxicity of medications. Of note, LiverTox does not provide detailed discussion on how medications are likely to impact persons with more advanced liver disease; for this inquiry, reviewing the drug package insert may be the best route. Commonly used medications, such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), are associated with an increased risk of gastrointestinal bleeding in persons with cirrhosis and should be avoided. It is important to identify any medication that may lead to nephrotoxicity in a person with decompensated cirrhosis, since this may cause them to develop hepatorenal syndrome.
- **Comorbid Medical Conditions**: A thorough medical history should be documented, including those diseases that might impact the progression of liver disease, such as HIV, hepatitis B, diabetes, obesity, and metabolic-associated steatotic liver disease (MASLD)—formerly referred to as nonalcoholic fatty liver disease or (NAFLD). These conditions can accelerate liver disease progression and all have enhanced importance in persons with chronic HCV infection and cirrhosis.
- **Review of Symptoms**: In patients with cirrhosis, it is critical to inquire about symptoms that would suggest complications of advanced liver disease, including abdominal girth swelling or tightness, lower extremity edema, jaundice, hematemesis or melena, and any signs of confusion or daytime somnolence.
- **Psychiatric History**: Chronic HCV infection may be associated with depression, and coexistent depression may lead to poorer survival.[18] Therefore, it is important to elicit a comprehensive mental health history.

Physical Examination

- **Body Mass Index (BMI)**: Height, weight, and the calculated body mass index (BMI) should be documented. Persons who are overweight (BMI greater than or equal to 25 kg/m^2) or obese (BMI greater than or equal to 30 kg/m^2) are at risk for MASLD.[19,20] In persons with chronic HCV infection, MASLD may contribute to and accelerate the development of cirrhosis.[21,22]
- **General Inspection**: Muscle wasting suggests advanced liver disease. Scleral icterus can usually be detected if the serum bilirubin level is greater than 3.0 mg/dL. Identifying jaundice is an important

factor in determining if a person has decompensated liver disease. Lower extremity edema can be an early sign of decompensated disease.

- **Peripheral Stigmata of Advanced Liver Disease**: Spider angiomata, also known as spider nevi or spider telangiectasias, represent anomalous dilatation of cutaneous blood vessels and are among the earliest physical examination signs of cirrhosis. Spider angiomata are most commonly seen on the anterior chest, neck, face, and upper thorax.[23] Palmar erythema, gynecomastia, and testicular atrophy can also be seen in advanced liver disease, and, like spider angiomata, are a reflection of impaired estrogen clearance. It is important to note that the absence of these findings is not sufficient to rule out cirrhosis.[23]
- **Abdominal Examination**: Examination of the abdomen may help determine the size of the liver and the presence of splenic enlargement, but the accuracy of physical examination in assessing organ size is limited.[8] The most useful physical examination findings to confirm ascites are the presence of a fluid wave and shifting dullness. The presence of flank dullness is highly sensitive and may be helpful in excluding clinically significant ascites.[24] For more detailed information about ascites, see the lesson Diagnosis and Management of Ascites.
- **Mental Status Assessment**: A brief general assessment of patient mental status is appropriate at each visit. For persons with suspected altered or impaired mental status, a formal assessment for hepatic encephalopathy should be performed. The mental status assessment for hepatic encephalopathy is addressed in detail in the lesson Diagnosis and Management of Hepatic Encephalopathy.

Classification Systems for Persons with Cirrhosis

Child-Turcotte-Pugh Score (CTP)

The Child-Turcotte classification system was developed in 1964 to risk-stratify patients undergoing shunt surgery for portal decompression.[25] In 1972, Pugh modified the Child-Turcotte system, and it became known as the Child-Turcotte-Pugh (CTP) score.[26] The CTP has been shown to predict survival and other clinical outcomes in persons with cirrhosis and portal hypertension.[14,27] Because it is simple and does not require complicated calculation, clinicians have widely used this tool to assess the risk of mortality in cirrhotic patients.[28] It is also the primary modality by which we distinguish between compensated versus decompensated liver disease.

- **Calculation**: The CTP scoring system incorporates two clinical parameters (encephalopathy and ascites) and three laboratory values (bilirubin, albumin, and prothrombin time) (Figure 3). Based on the sum of the points from these five parameters, the person is categorized into one of three CTP classes: A, B, or C. The CTP Calculator automatically computes the CTP score based on the data entered.
- **Limitations**: The CTP score has several limitations. First, the score has limited discriminatory capacity and does not adequately account for the degree of abnormal lab results.[28,29] For example, a person with a serum bilirubin of 20 mg/dL would be assigned the same number of points as a person with a serum bilirubin of 3.5 mg/dL even though an extremely high serum bilirubin has poorer prognostic impact.[29] Second, the CTP score gives equal weight to each of the five variables, which has been questioned by some experts.[28,29] Third, the two clinical parameters—ascites and encephalopathy—are vulnerable to subjective interpretation. Fourth, some important prognostic factors, including serum sodium, serum creatinine, and variceal hemorrhage, are not included in the CTP scoring system.[28,29]
- **Clinical Use:** The CTP score is still widely used in the clinic and hospital setting as a simple prognostic tool. Studies involving persons with cirrhosis have shown that CTP scores can estimate survival at 3 months, as well as 1- to 2-year survival (Figure 4).[14,30] For persons with cirrhosis, most experts recommend assessing the CTP score at each clinical visit. The CTP score was previously used as a major criterion for liver transplantation evaluation, but it is no longer widely used for this purpose.[16]

Model for End-stage Liver Disease (MELD)

The Model for End-Stage Liver Disease (MELD) score was originally developed to predict the survival of persons with advanced liver disease who underwent an elective transjugular intrahepatic portosystemic shunt (TIPS) procedure.[31] Investigators then studied the MELD scoring system in other individuals with cirrhosis and found it to be a good predictor of mortality in persons who did not have TIPS placed; with the MELD score, the higher the score, the higher the 90-day mortality (and lower the 90-day survival) (Figure 5).[30,32,33] The MELD score was adopted in 2002 by the United Network for Organ Sharing (UNOS) to prioritize allocation of deceased donor organs for liver transplantation.[34] The MELD score has undergone several iterations, with the most recent version being the MELD 3.0.[35]

MELD 3.0

The MELD 3.0 version, which also incorporates sex (male or female) and albumin level, affords more accurate mortality prediction, in general, than the prior version, MELDNa.[35] With MELD 3.0, similar to prior versions of MELD, the higher the score, the lower the 90-day survival.[30] For example, a person with a MELD 3.0 score less than or equal to 15 has a predicted 3-month survival of 98%, whereas an individual with a MELD score of 30 has a predicted 3-month survival of only 73%.[35]

- **Calculation of MELD 3.0 Score**: The MELD 3.0 score, which estimates the survival probability of a

patient with end-stage liver disease, is based on sex (male or female) and several commonly obtained laboratory tests, including serum bilirubin, serum creatinine, and international normalized ratio (INR), serum sodium, and serum albumin.[35] The MELD 3.0 Calculator will compute the MELD 3.0 score based on the variable entered.

- **Limitations**: The MELD 3.0 score can be influenced by the method in which serum creatinine and INR are measured across laboratories.[28,29,35] When compared with the CTP scoring system, the MELD 3.0 score has an advantage in its use of objective data, and it can distinguish disease severity along a continuous spectrum.[35] Earlier versions of the MELD scoring system have been reported to have a misclassification rate of up to 10 to 20%.[28]
- **Clinical Use**: The MELD 3.0 score should be calculated on any person with cirrhosis or advanced liver disease at each clinic visit. Individuals with cirrhosis and a MELD 3.0 score of 15 or greater should be referred for a liver transplantation evaluation.[16,35]

Compensated Cirrhosis

Definition and Natural History

Cirrhosis is considered to be compensated in the asymptomatic patient with or without gastroesophageal varices. Child-Turcotte-Pugh scores of these individuals are generally in class A (6 or less). Persons with compensated cirrhosis are not jaundiced and have not yet developed ascites, variceal bleeding, or hepatic encephalopathy.[14,36] Cirrhosis can remain compensated for many years.[36] The transition from compensated to decompensated cirrhosis occurs at a rate of approximately 5 to 7% per year overall, including among patients with untreated chronic HCV.[14,37] The median survival of persons with compensated cirrhosis is approximately 9 to 12 years.[14]

Surveillance for Hepatocellular Carcinoma

The development of cirrhosis is the single most important risk factor for developing hepatocellular carcinoma (HCC).[38,39] Accordingly, all persons with cirrhosis (compensated or decompensated) should undergo surveillance for HCC with hepatic ultrasound, with or without serum alpha-fetoprotein (AFP), every 6 months.[9,16] For patients with chronic HCV infection and cirrhosis, surveillance for HCC should continue after treatment for HCV, even if the individual obtained a sustained virologic response.[40] Some experts also recommend surveillance for HCC in persons with chronic HCV infection and Metavir stage F3 (stage before cirrhosis), although the data in support of screening in this subpopulation are limited.[41,42]

Screening for Gastroesophageal Varices

Among persons with cirrhosis, gastroesophageal varices develop at a rate of approximately 8% per year, and varices often develop initially without causing any symptoms or bleeding.[36] All patients with cirrhosis should undergo screening for gastroesophageal varices with transient elastography as a method for risk stratifications or an upper endoscopy to identify those individuals who may benefit from taking a nonselective beta-blocker for prophylaxis.[6,9,43] The subsequent assessment and management is based on the findings at endoscopy and is discussed in detail in Module 3, in the lesson Screening for Varices and Prevention of Bleeding.

Treatment of HCV in Patients with Compensated Cirrhosis

The major goal of managing patients with HCV and compensated cirrhosis is to treat the HCV infection.[44,45] Treatment of HCV in patients with compensated cirrhosis using direct-acting antiviral (DAA) medications has been associated with sustained virologic response (SVR) rates of 90% or better.[46,47,48,49] Patients with HCV-related cirrhosis who undergo treatment and achieve a cure have a dramatically decreased 10-year risk of all-cause mortality (hazard ratio [HR] = 0.26), liver-related mortality or transplantation (HR = 0.06), hepatocellular carcinoma (HR = 0.19), and hepatic decompensation (HR = 0.07).[45] For a more detailed discussion of this topic, see the lesson Treatment of HCV in Persons with Cirrhosis.

Decompensated Cirrhosis

Definition and Natural History

Decompensated cirrhosis is defined by a calculated CTP score of 7 to 15 (CTP Class B or C) and is often accompanied by the development of jaundice, ascites, variceal hemorrhage, and/or hepatic encephalopathy.[14] The survival of persons with decompensated liver disease is significantly lower than in those with compensated disease. A MELD score should be calculated for all persons with decompensated cirrhosis to better estimate the survival probability and to determine eligibility for transplantation. Evaluation for transplantation should be considered once a person is diagnosed with decompensated cirrhosis or has a MELD score of 15 or greater.[16]

Treatment of HCV in Patients with Decompensated Cirrhosis

Treatment of HCV in persons with decompensated cirrhosis has become possible with all-oral DAA therapy. Moderately high rates of sustained virologic response rates have been demonstrated with DAA therapy in persons with decompensated cirrhosis.[50,51,52,53] Treatment of HCV in persons with decompensated cirrhosis should be managed either by a hepatologist or with the very close involvement of a hepatologist. For individuals with chronic HCV and decompensated cirrhosis who are liver transplantation candidates, successful treatment of HCV with DAA therapy has occurred before and after transplantation.[54,55,56] Given the complexity of these situations, decisions regarding the approach to HCV treatment and optimal timing of HCV treatment (before or after the transplant) should be made by the liver transplantation team.

Ascites

Ascites is the pathologic accumulation of fluid in the peritoneal cavity and a manifestation of portal hypertension in cirrhosis. It is the most common and often the first complication of cirrhosis for many individuals, with approximately 5-10% of individuals with compensated cirrhosis developing ascites per year.[57] The development of ascites results in a significant drop in survival by 50% due to other life-threatening complications, such as hepatorenal syndrome or infections, that may ensue.[57] Although treatment of ascites does not result in enhanced survival, it does improve the individual's quality of life and decreases the risk of developing spontaneous bacterial peritonitis (SBP). This topic is addressed in greater detail in the lesson Diagnosis and Management of Ascites.

Spontaneous Bacterial Peritonitis (SBP)

Among persons with cirrhosis and ascites, SBP is the most common infectious complication, accounting for 27% of bacterial infections in hospitalized patients.[57,58] The recurrence rate of SBP after an initial episode is very high (approximately 70%) without prophylaxis. Persons who survive an initial episode of SBP should receive antibiotic prophylaxis. This topic is addressed in greater detail in the lesson Recognition and Management of Spontaneous Bacterial Peritonitis.

Variceal Hemorrhage

The rate of bleeding with known varices is estimated to be 10 to 30% per year, depending on the size of the varices and underlying severity of liver disease.[9] The mortality rate from each episode of variceal hemorrhage is approximately 15%.[59,60] Acute variceal bleeding is a medical emergency and requires control of bleeding and prevention of complications.[60] The risk of rebleeding within 1 year of the initial bleed is approximately 60%.[61] Thus, it is extremely important that persons who survive an initial variceal hemorrhage start prophylactic therapy to prevent future bleeds.[60] Recommendations regarding primary prophylaxis, secondary prophylaxis, and management of variceal bleeding are discussed in greater detail in the lesson Screening for Varices and Prevention of Bleeding.

Hepatic Encephalopathy

Hepatic encephalopathy is thought to result from a buildup of toxic compounds generated by gut bacteria.[62] In a normal liver, these compounds are transported through the portal vein to the liver and metabolized and excreted immediately. In persons with cirrhosis, however, these toxins are not metabolized properly. Individuals who develop hepatic encephalopathy may have subtle symptoms, and the onset is often insidious. Hepatic encephalopathy represents a continuum from minimal to overt and can be episodic or persistent. This topic is addressed in greater detail in the lesson Diagnosis and Management of Hepatic Encephalopathy.

Hepatorenal Syndrome

Hepatorenal syndrome is defined as renal failure in a person with cirrhosis in the absence of intrinsic renal disease.[63] The pathophysiology of hepatorenal syndrome is not completely understood, but it is thought to occur secondary to underfilling of the arterial circulation because of arterial vasodilation in the splanchnic circulation.[64] This causes sodium and water retention, with renal vasoconstriction, which results in decreased renal blood flow and urinary output. Some experts have noted that use of beta-blockers in persons with decompensated cirrhosis may increase the risk of hepatorenal syndrome, and many experts recommend discontinuing or avoiding the use of beta-blockers in persons with cirrhosis who have developed hepatorenal syndrome.[65,66,67] Hepatorenal syndrome has historically been divided into 2 types: type 1 and type 2.[63,64,68,69] These terms have since been replaced by the terms hepatorenal syndrome acute injury and hepatorenal syndrome chronic kidney disease, respectively.[64,70]

Summary Points

- Persons with decompensated cirrhosis have complications related to cirrhosis (e.g., jaundice, ascites, variceal hemorrhage, and/or hepatic encephalopathy.
- Most individuals with chronic HCV infection will have a normal physical examination, but those with advanced liver disease may have findings that suggest cirrhosis.
- The CTP scoring system is based on five parameters (serum bilirubin, serum albumin, prothrombin time, severity of ascites, and grade of encephalopathy); it is easy to calculate and provides valuable prognostic information.
- The MELD score provides accurate short-term prognostic information and should be calculated on any person with cirrhosis. Individuals with a MELD score greater than or equal to 15 or decompensated cirrhosis, should be considered for a liver transplantation evaluation.
- Management of persons with chronic HCV infection and compensated cirrhosis should include treatment of the HCV infection.
- Decompensated cirrhosis is defined by a CTP score of 7 or greater and is often accompanied by the development of jaundice, ascites, variceal hemorrhage, or hepatic encephalopathy.
- Survival is poor in persons with decompensated cirrhosis, and they should be considered for liver transplantation.

Citations

1. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. Nat Rev Gastroenterol Hepatol. 2013;10:553-62.
[PubMed Abstract] -

2. Liang TJ, Rehermann B, Seeff LB, Hoofnagle JH. Pathogenesis, natural history, treatment, and prevention of hepatitis C. Ann Intern Med. 2000;132:296-305.
[PubMed Abstract] -

3. Lingala S, Ghany MG. Natural History of Hepatitis C. Gastroenterol Clin North Am. 2015;44:717-34.
[PubMed Abstract] -

4. Starr SP, Raines D. Cirrhosis: diagnosis, management, and prevention. Am Fam Physician. 2011;84:1353-9.
[PubMed Abstract] -

5. Brunner F, Berzigotti A, Bosch J. Prevention and treatment of variceal haemorrhage in 2017. Liver Int. 2017;37 Suppl 1:104-115.
[PubMed Abstract] -

6. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362:823-32.
[PubMed Abstract] -

7. Ge PS, Runyon BA. Treatment of Patients with Cirrhosis. N Engl J Med. 2016;375:767-77.
[PubMed Abstract] -

8. de Bruyn G, Graviss EA. A systematic review of the diagnostic accuracy of physical examination for the detection of cirrhosis. BMC Med Inform Decis Mak. 2001;1:6.
[PubMed Abstract] -

9. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology. 2017;65:310-335.
[PubMed Abstract] -

10. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician.2006;74:756-62.
[PubMed Abstract] -

11. Planas R, Ballesté B, Alvarez MA, et al. Natural history of decompensated hepatitis C virus-related cirrhosis. J Hepatol. 2004;40:823-30.
[PubMed Abstract] -

12. Garcia-Tsao G, Friedman S, Iredale J, Pinzani M. Now there are many (stages) where before there was one: In search of a pathophysiological classification of cirrhosis. Hepatology. 2010;51:1445-9.
[PubMed Abstract] -

13. Zipprich A, Garcia-Tsao G, Rogowski S, Fleig WE, Seufferlein T, Dollinger MM. Prognostic indicators of survival in patients with compensated and decompensated cirrhosis. Liver Int. 2012;32:1407-14.
[PubMed Abstract] -

14. 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] -

15. Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: a population-based cohort study. Liver Int. 2012;32:79-84.
[PubMed Abstract] -

16. 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] -

17. Wiley TE, McCarthy M, Breidi L, McCarthy M, Layden TJ. Impact of alcohol on the histological and clinical progression of hepatitis C infection. Hepatology. 1998;28:805-9.
[PubMed Abstract] -

18. Adinolfi LE, Nevola R, Rinaldi L, Romano C, Giordano M. Chronic Hepatitis C Virus Infection and Depression. Clin Liver Dis. 2017;21:517-534.
[PubMed Abstract] -

19. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79:1542-56.
[PubMed Abstract] -

20. Vargas M, Cardoso Toniasso SC, Riedel PG, et al. Metabolic disease and the liver: A review. World J Hepatol. 2024;16:33-40.
[PubMed Abstract] -

21. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015;313:2263-73.
[PubMed Abstract] -

22. Leslie J, Geh D, Elsharkawy AM, Mann DA, Vacca M. Metabolic dysfunction and cancer in HCV: Shared pathways and mutual interactions. J Hepatol. 2022;77:219-36.
[PubMed Abstract] -

23. Udell JA, Wang CS, Tinmouth J, et al. Does this patient with liver disease have cirrhosis? JAMA. 2012;307:832-42.
[PubMed Abstract] -

24. Cattau EL Jr, Benjamin SB, Knuff TE, Castell DO. The accuracy of the physical examination in the diagnosis of suspected ascites. JAMA. 1982;247:1164-6.
[PubMed Abstract] -

25. Child CG, Turcotte JG. Surgery and portal hypertension. Major Probl Clin Surg. 1964;1:1-85.
[PubMed Abstract] -

26. 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] -

27. D'Amico G, Morabito A, Pagliaro L, Marubini E. Survival and prognostic indicators in compensated and decompensated cirrhosis. Dig Dis Sci. 1986;31:468-75.
[PubMed Abstract] -

28. Durand F, Valla D. Assessment of prognosis of cirrhosis. Semin Liver Dis. 2008;28:110-22.
[PubMed Abstract] -

29. Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD. J Hepatol. 2005;42 Suppl:S100-7.
[PubMed Abstract] -

30. 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] -

31. 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] -

32. Bruno S, Zuin M, Crosignani A, et al. Predicting mortality risk in patients with compensated HCV-induced cirrhosis: a long-term prospective study. Am J Gastroenterol. 2009;104:1147-58.
[PubMed Abstract] -

33. 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] -

34. Freeman RB Jr, Wiesner RH, Harper A, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl. 2002;8:851-8.
[PubMed Abstract] -

35. Kim WR, Mannalithara A, Heimbach JK, et al. MELD 3.0: The Model for End-Stage Liver Disease Updated for the Modern Era. Gastroenterology. 2021;161:1887-95.
[PubMed Abstract] -

36. D'Amico G, Morabito A, D'Amico M, et al. Clinical states of cirrhosis and competing risks. J Hepatol. 2018;68:563-576.
[PubMed Abstract] -

37. Di Bisceglie AM, Shiffman ML, Everson GT, et al. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. N Engl J Med. 2008;359:2429-41.
[PubMed Abstract] -

38. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterol. 2007;132:2557-76.
[PubMed Abstract] -

39. Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet. 2018;391:1301-1314.
[PubMed Abstract] -

40. AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Monitoring patients who are starting HCV treatment, are on treatment, or have completed therapy.
[AASLD-IDSA HCV Guidance] -

41. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2018;68:723-50.

[PubMed Abstract] -

42. Ioannou GN. HCC surveillance after SVR in patients with F3/F4 fibrosis. J Hepatol. 2021;74:458-65. [PubMed Abstract] -

43. Thiele M, Johansen S, Israelsen M, et al. Non-invasive assessment of hepatic decompensation. Hepatology. 2023 Oct 6. Online ahead of print. [PubMed Abstract] -

44. Singal AG, Volk ML, Jensen D, Di Bisceglie AM, Schoenfeld PS. A sustained viral response is associated with reduced liver-related morbidity and mortality in patients with hepatitis C virus. Clin Gastroenterol Hepatol. 2010;8:280-8. [PubMed Abstract] -

45. van der Meer AJ, Veldt BJ, Feld JJ, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA. 2012 ;308:2584-93. [PubMed Abstract] -

46. Asselah T, Kowdley KV, Zadeikis N, et al. Efficacy of Glecaprevir/Pibrentasvir for 8 or 12 Weeks in Patients With Hepatitis C Virus Genotype 2, 4, 5, or 6 Infection Without Cirrhosis. Clin Gastroenterol Hepatol. 2018;16:417-26. [PubMed Abstract] -

47. Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. N Engl J Med. 2015;373:2599-607. [PubMed Abstract] -

48. Forns X, Lee SS, Valdes J, et al. Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis (EXPEDITION-1): a single-arm, open-label, multicentre phase 3 trial. Lancet Infect Dis. 2017;17:1062-1068. [PubMed Abstract] -

49. Lawitz E, Gane E, Pearlman B, et al. Efficacy and safety of 12 weeks versus 18 weeks of treatment with grazoprevir (MK-5172) and elbasvir (MK-8742) with or without ribavirin for hepatitis C virus genotype 1 infection in previously untreated patients with cirrhosis and patients with previous null response with or without cirrhosis (C-WORTHY): a randomised, open-label phase 2 trial. Lancet. 2015;385:1075-86. [PubMed Abstract] -

50. Foster GR, Irving WL, Cheung MC, et al. Impact of direct acting antiviral therapy in patients with chronic hepatitis C and decompensated cirrhosis. J Hepatol. 2016;64:1224-31. [PubMed Abstract] -

51. Cheung MCM, Walker AJ, Hudson BE, et al. Outcomes after successful direct-acting antiviral therapy for patients with chronic hepatitis C and decompensated cirrhosis. J Hepatol. 2016;65:741-747. [PubMed Abstract] -

52. Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. N Engl J Med. 2015;373:2618-28. [PubMed Abstract] -

53. Manns M, Samuel D, Gane EJ, et al. Ledipasvir and sofosbuvir plus ribavirin in patients with genotype 1 or 4 hepatitis C virus infection and advanced liver disease: a multicentre, open-label, randomised,

phase 2 trial. Lancet Infect Dis. 2016;16:685-97.
[PubMed Abstract] -

54. Bunchorntavakul C, Reddy KR. Treat chronic hepatitis C virus infection in decompensated cirrhosis - pre- or post-liver transplantation? the ironic conundrum in the era of effective and well-tolerated therapy. J Viral Hepat. 2016;23:408-18.
[PubMed Abstract] -

55. Cholankeril G, Joseph-Talreja M, Perumpail BJ, et al. Timing of Hepatitis C Virus Treatment in Liver Transplant Candidates in the Era of Direct-acting Antiviral Agents. J Clin Transl Hepatol. 2017;5:363-367.
[PubMed Abstract] -

56. Gadiparthi C, Cholankeril G, Perumpail BJ, et al. Use of direct-acting antiviral agents in hepatitis C virus-infected liver transplant candidates. World J Gastroenterol. 2018;24:315-322.
[PubMed Abstract] -

57. Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74:1014-48.
[PubMed Abstract] -

58. Piano S, Singh V, Caraceni P, et al. Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide. Gastroenterology. 2019;156:1368-80.
[PubMed Abstract] -

59. Krige JE, Kotze UK, Distiller G, Shaw JM, Bornman PC. Predictive factors for rebleeding and death in alcoholic cirrhotic patients with acute variceal bleeding: a multivariate analysis. World J Surg. 2009;33:2127-35.
[PubMed Abstract] -

60. Kaplan DE, Bosch J, Ripoll C, et al. AASLD practice guidance on risk stratification and management of portal hypertension and varices in cirrhosis. Hepatology. 2023 Oct 23. Online ahead of print.
[PubMed Abstract] -

61. Haq I, Tripathi D. Recent advances in the management of variceal bleeding. Gastroenterol Rep (Oxf). 2017;5:113-126.
[PubMed Abstract] -

62. Prakash R, Mullen KD. Mechanisms, diagnosis and management of hepatic encephalopathy. Nat Rev Gastroenterol Hepatol. 2010;7:515-25.
[PubMed Abstract] -

63. Salerno F, Gerbes A, Ginès P, Wong F, Arroyo V. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. Gut. 2007;56:1310-8.
[PubMed Abstract] -

64. Wong F. The evolving concept of acute kidney injury in patients with cirrhosis. Nat Rev Gastroenterol Hepatol. 2015;12:711-9.
[PubMed Abstract] -

65. Ge PS, Runyon BA. The changing role of beta-blocker therapy in patients with cirrhosis. J Hepatol. 2014;60:643-53.
[PubMed Abstract] -

66. Mandorfer M, Bota S, Schwabl P, et al. Nonselective β blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology. 2014;146:1680-90.e1.
[PubMed Abstract] -

67. Mandorfer M, Reiberger T. Beta blockers and cirrhosis, 2016. Dig Liver Dis. 2017;49:3-10.
[PubMed Abstract] -

68. Shah N, Silva RG, Kowalski A, Desai C, Lerma E. Hepatorenal syndrome. Dis Mon. 2016;62:364-375.
[PubMed Abstract] -

69. Baraldi O, Valentini C, Donati G, et al. Hepatorenal syndrome: Update on diagnosis and treatment. World J Nephrol. 2015;4:511-20.
[PubMed Abstract] -

70. Angeli P, Gines P, Wong F, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. Gut. 2015;64:531-7.
[PubMed Abstract] -

References

- Acharya C, Sahingur SE, Bajaj JS. Microbiota, cirrhosis, and the emerging oral-gut-liver axis. JCI Insight. 2017;2:e94416.
[PubMed Abstract] -

- Bini EJ, Bräu N, Currie S, et al. Prospective multicenter study of eligibility for antiviral therapy among 4,084 U.S. veterans with chronic hepatitis C virus infection. Am J Gastroenterol. 2005;100:1772-9.
[PubMed Abstract] -

- D'Amico G, Morabito A, D'Amico M, et al. New concepts on the clinical course and stratification of compensated and decompensated cirrhosis. Hepatol Int. 2018;12:34-43.
[PubMed Abstract] -

- D’Amico G, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology. 2003;38:599-612.
[PubMed Abstract] -

- Garcia-Tsao G, Lim JK; Members of Veterans Affairs Hepatitis C Resource Center Program. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. Am J Gastroenterol. 2009;104:1802-29.
[PubMed Abstract] -

- Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. Gastroenterology. 2001;120:726-48.
[PubMed Abstract] -

- Hézode C, Roudot-Thoraval F, Nguyen S, et al. Daily cannabis smoking as a risk factor for progression of fibrosis in chronic hepatitis C. Hepatology. 2005;42:63-71.
[PubMed Abstract] -

- 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] -

- Maier MM, He H, Schafer SD, Ward TT, Zaman A. Hepatitis C treatment eligibility among HIV-hepatitis C virus coinfected patients in Oregon: a population-based sample. AIDS Care. 2014;26:1178-85.
  [PubMed Abstract] -

- Morgan TR, Ghany MG, Kim HY, et al. Outcome of sustained virological responders with histologically advanced chronic hepatitis C. Hepatology. 2010;52:833-44.
  [PubMed Abstract] -

- Sheer TA, Runyon BA. Spontaneous bacterial peritonitis. Dig Dis. 2005;23:39-46.
  [PubMed Abstract] -

- Williams JW Jr, Simel DL. The rational clinical examination. Does this patient have ascites? How to divine fluid in the abdomen. JAMA. 1992;267:2645-8.
  [PubMed Abstract] -

Figures

Figure 1 Four-Stage Cirrhosis Classification System

In this figure, bleeding refers to variceal bleeding. The risk of death increases significantly with each more advanced stage.

Source: 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.

	Compensated Cirrhosis		Decompensated Cirrhosis	
Stage	Stage 1	Stage 2	Stage 3	Stage 4
Clinical	No Varices No Ascites	Varices No Ascites	Ascites +/- Varices	Bleeding +/- Ascites
Death (at 1 Year)	1%	3%	20%	57%

Figure 2 (Image Series) - Survival with Compensated or Decompensated Cirrhosis (Image Series) - Figure 2 (Image Series) - Survival with Compensated or Decompensated Cirrhosis
Image 2A: One- and Two-Year Survival Rates

In this study, investigators analyzed data from 18 studies in patients with compensated cirrhosis and 23 studies in patients with decompensated cirrhosis to estimate 1- and 2-year survival rates.

Source: 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.

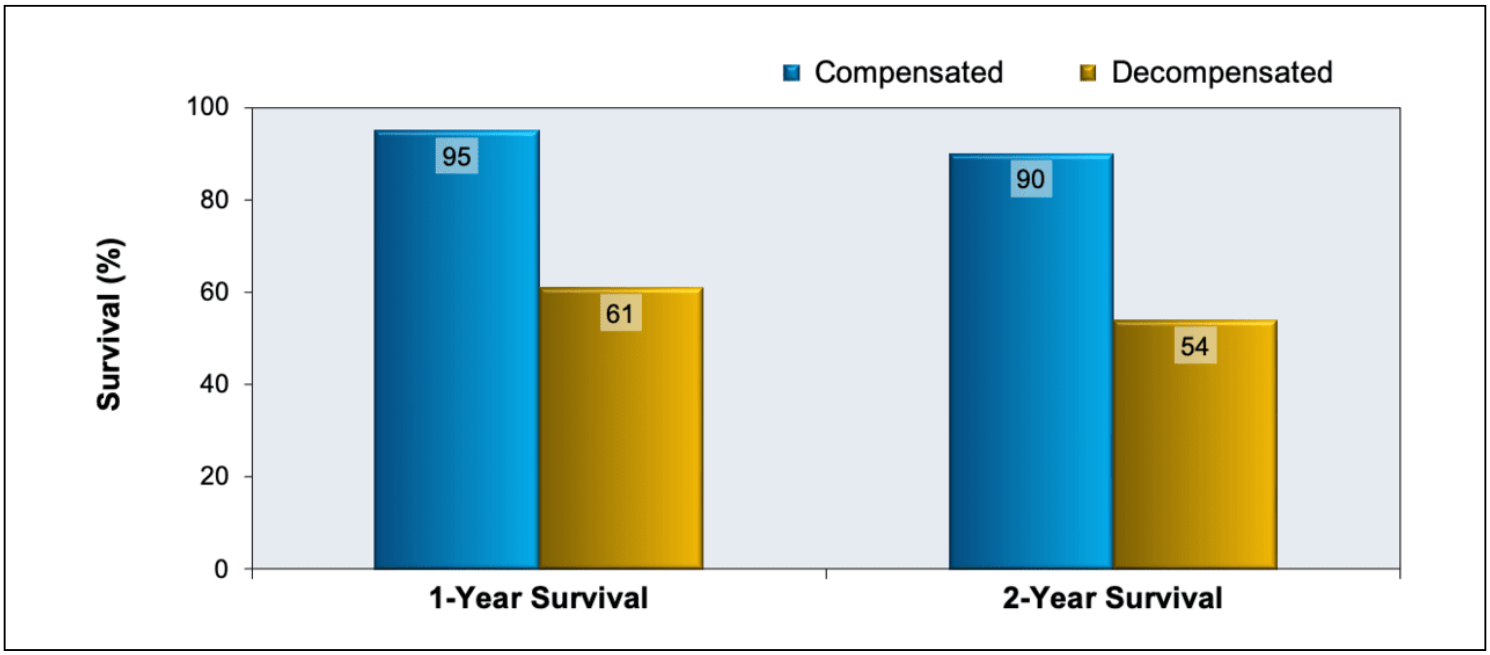


Figure 2 (Image Series) - Survival with Compensated or Decompensated Cirrhosis
Image 2B: One- and Five-Year Survival Rates

This study evaluated mortality rates in 4,537 persons with cirrhosis in the United Kingdom during the years 1987 and 2002.

Source: Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: a population-based cohort study. Liver Int. 2012;32:79-84.

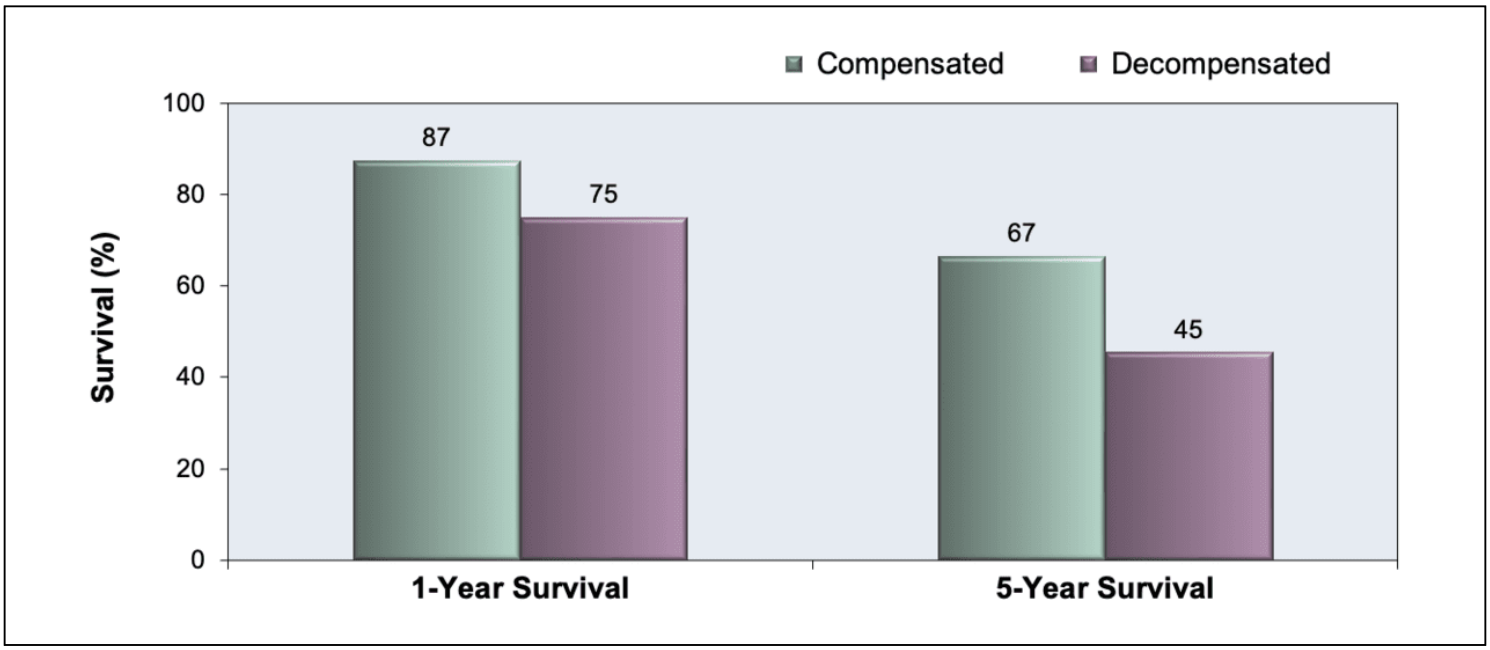


Figure 3 Child-Turcotte-Pugh Classification for Severity of Cirrhosis

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

	Points*		
	1	2	3
Encephalopathy	None	Grade 1-2 (or precipitant induced)	Grade 3-4 (or chronic)
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
INR	<1.7	1.7-2.3	>2.3

***Child-Turcotte-Pugh Class and liver disease severity obtained by adding score for each parameter (total points)**

Class A = 5 to 6 points (least severe); **Class B** = 7 to 9 points (moderately severe); **Class C** = 10 to 15 points (most severe)

Figure 4 (Image Series) - Survival Based on Child-Turcotte-Pugh Score (Image Series) - Figure 4 (Image Series) - Survival Based on Child-Turcotte-Pugh Score
Image 4A: Survival at 3 Months Based on Child-Turcotte-Pugh Score

Patients 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.

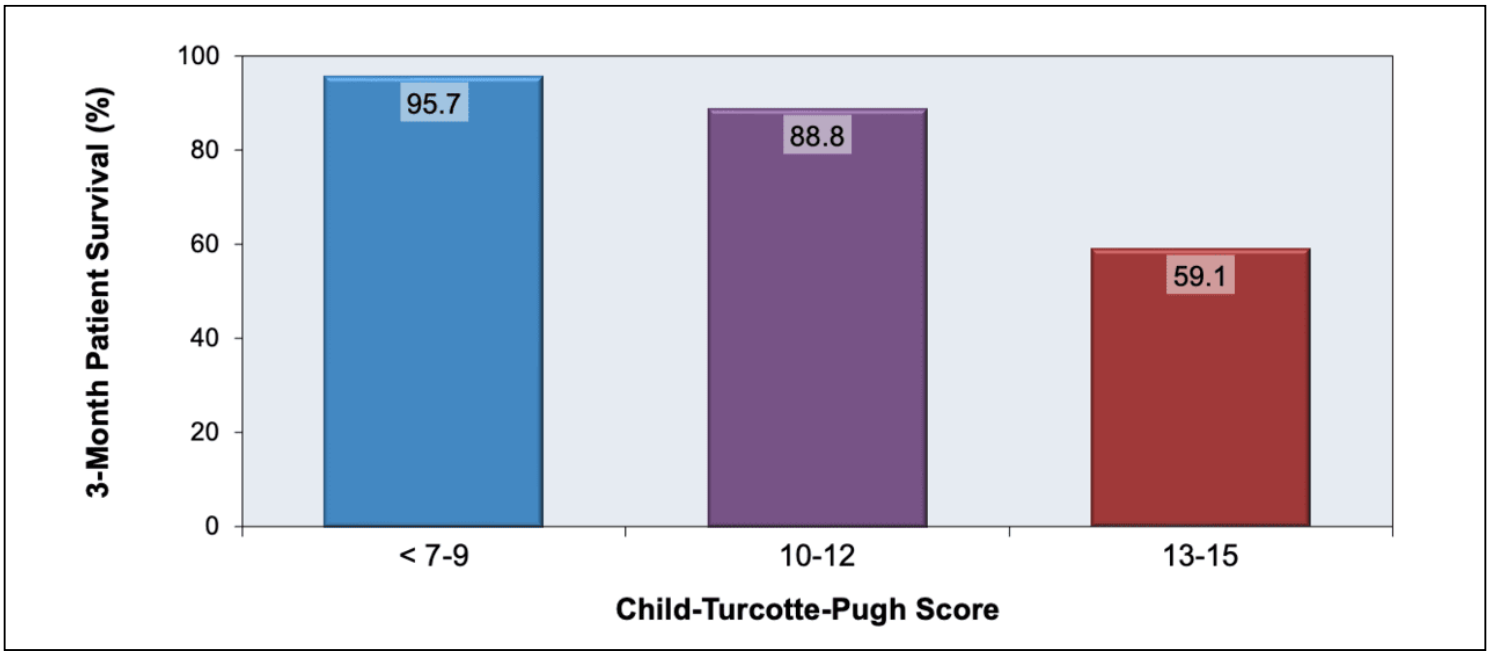


Figure 4 (Image Series) - Survival Based on Child-Turcotte-Pugh Score
Image 4B: Survival at 1 and 2 Years Based on Child-Pugh Score

This graphic shows a clear relationship of baseline Child-Pugh class (A, B, or C) and survival at 1 or 2 years. Without liver transplantation, patients with class C have a 1-year survival less than 50%.

Source: 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.

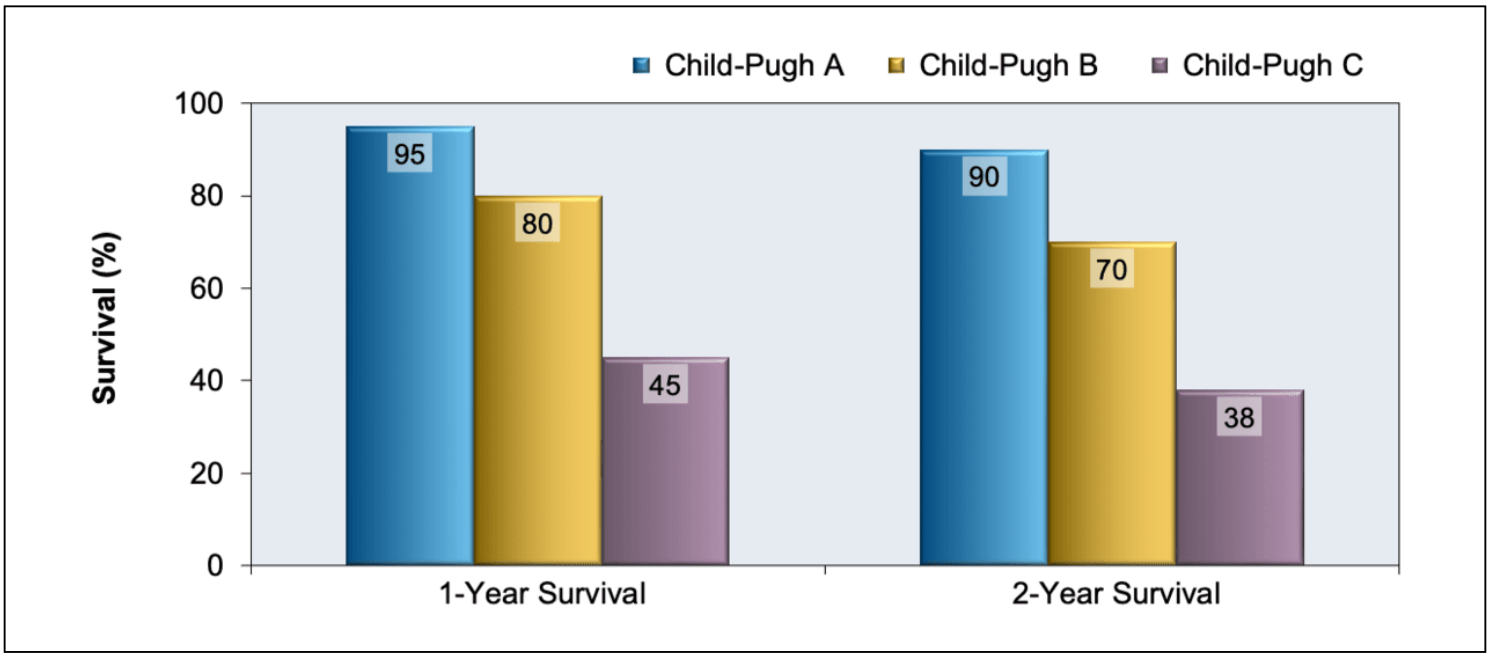
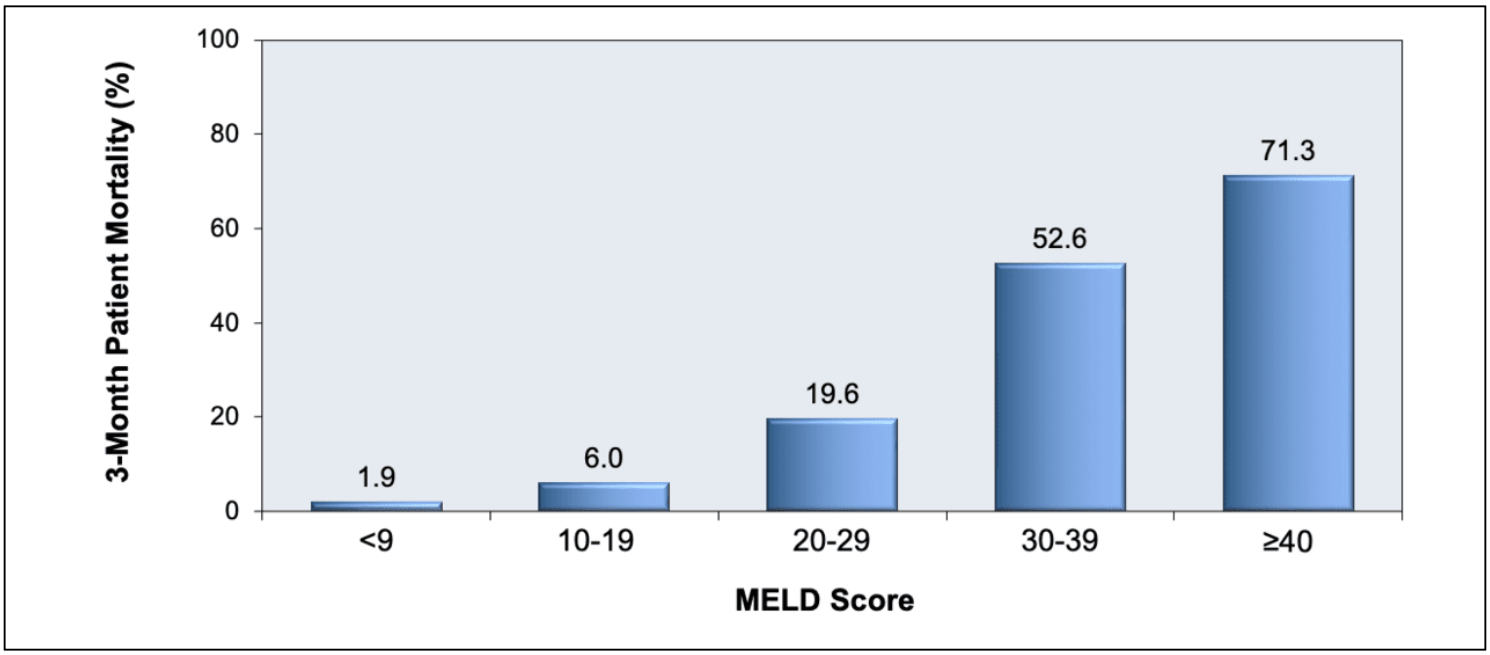


Figure 5 Morality at 3 Months Based on MELD Score

This graphic shows that with each 10-point increase in MELD score the 3-month mortality goes up significantly. Individuals with a MELD score greater than 30 have a 3-month mortality that exceeds 50%. Abbreviations: MELD = Model for End-Stage Liver Disease

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.