Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis

AUTHORS: Eric Goldberg, MD, Sanjiv Chopra, MD, MACP
SECTION EDITOR: Bruce A Runyon, MD, FAASLD
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Mar 2024.**
This topic last updated: **Jan 23, 2023.**

INTRODUCTION

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages, at which point the only treatment option may be liver transplantation. However, reversal of cirrhosis (in its earlier stages) has been documented in several forms of liver disease following treatment of the underlying cause. Patients with cirrhosis are susceptible to a variety of complications, and their life expectancy is markedly reduced. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Prognosis'.)

This topic will review the etiologies, clinical manifestations, and diagnosis of cirrhosis. An overview of the complications, prognosis, and general management of cirrhosis is discussed separately. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis".)

ETIOLOGIES AND CLASSIFICATION

There are numerous causes of liver disease that can result in cirrhosis, either by causing chronic hepatic inflammation or cholestasis. The most common causes of cirrhosis in the United States are hepatitis C, alcohol-associated liver disease, and nonalcohol-associated liver disease, which together accounted for approximately 80 percent of patients on the liver transplantation waitlist between 2004 and 2013 [1].

In developed countries, common causes of cirrhosis include [2]:

- Chronic viral hepatitis (hepatitis B, C)
- Alcohol-associated liver disease
- Hemochromatosis
- Nonalcohol-associated fatty liver disease

Less common causes include:

- Autoimmune hepatitis
- Primary and secondary biliary cirrhosis
- Primary sclerosing cholangitis
- Medications (eg, methotrexate, isoniazid)
- Wilson disease
- Alpha-1 antitrypsin deficiency
- Celiac disease
- Idiopathic adulthood ductopenia
- Granulomatous liver disease
- Idiopathic portal fibrosis
- Polycystic liver disease
- Infection (eg, brucellosis, syphilis, echinococcosis)
- Right-sided heart failure
- Hereditary hemorrhagic telangiectasia
- Veno-occlusive disease

Cirrhosis was historically classified morphologically as micronodular, macronodular, or mixed [3]. Micronodular cirrhosis, characterized by nodules less than 3 mm in diameter, was believed to be caused by alcohol, hemochromatosis, cholestatic causes of cirrhosis, and hepatic venous outflow obstruction. Macronodular cirrhosis, characterized by various sized nodules larger than 3 mm, was believed to be secondary to chronic viral hepatitis.

Although important from a historic perspective, the morphological classification system has a number of limitations and has thus largely been abandoned. First, it is relatively nonspecific with regard to etiology. Second, the morphologic appearance of the liver may change as the liver disease progresses; micronodular cirrhosis usually progresses to macronodular cirrhosis [4]. Third, serological markers available today are more specific than morphological appearance of the liver for determining the etiology of cirrhosis. As an example, antimitochondrial antibodies have a specificity of 98 percent for primary biliary cholangitis [5]. Finally, accurate assessment of liver morphology can only be achieved at surgery, laparoscopy, or autopsy, while in today's clinical practice there are less invasive means to make an etiologic diagnosis.

CLINICAL MANIFESTATIONS

The clinical manifestations of cirrhosis may include nonspecific symptoms (eg, anorexia, weight loss, weakness, fatigue) or signs and symptoms of hepatic decompensation (jaundice, pruritus, signs of upper gastrointestinal bleeding, abdominal distension from ascites, confusion due to hepatic encephalopathy) (table 1). Physical examination findings may include jaundice, spider angiomata, gynecomastia, ascites, splenomegaly, palmar erythema, digital clubbing, and asterixis. Laboratory abnormalities may include elevated serum bilirubin, abnormal aminotransferases, elevated alkaline phosphatase/gamma-glutamyl transpeptidase, a prolonged prothrombin time/elevated international normalized ratio (INR), hyponatremia, hypoalbuminemia, and thrombocytopenia.

Symptoms — Patients with compensated cirrhosis may be asymptomatic or they may report nonspecific symptoms, such as anorexia, weight loss, weakness, and fatigue. Patients with decompensated cirrhosis may present with jaundice, pruritus, signs of upper gastrointestinal bleeding (hematemesis, melena, hematochezia), abdominal distension from ascites, or confusion due to hepatic encephalopathy. Patients with cirrhosis may experience muscle cramps, which can be severe [6-10]. The cause is incompletely understood, although they may be related to a reduction in effective circulating plasma volume.

Patients should be asked about fatigue, easy bruisability, lower extremity edema, fever, weight loss, diarrhea, pruritus, increasing abdominal girth, confusion, or sleep disturbances (possibly indicating encephalopathy). The cause of diarrhea in patients with cirrhosis may be multifactorial (eg, alterations in small bowel motility, small bowel bacterial overgrowth, changes in intestinal permeability and bile acid deficiency) [11].

In women, chronic anovulation is common, which may manifest as amenorrhea or irregular menstrual bleeding [12]. Some of the abnormalities may be due to variations in testosterone, estradiol, prolactin, and luteinizing hormone levels in patients with cirrhosis compared with normal controls [13].

Men with cirrhosis may develop hypogonadism. It is manifested by impotence, infertility, loss of sexual drive, and testicular atrophy. It is a feature seen predominantly in patients with alcoholic cirrhosis and hemochromatosis. More than one mechanism appears to be involved. In some cases, primary gonadal injury appears to be more prominent, as suggested by increased serum follicle stimulating hormone (FSH) and luteinizing hormone (LH) concentrations, whereas in others, suppression of hypothalamic or pituitary function appears to have a primary role, as suggested by serum LH concentrations that are not elevated. The toxic effects of alcohol or iron may also contribute to its development [14]. (See "Causes of primary hypogonadism in males".)

Patients with cirrhosis may also present with a diverse range of signs and symptoms that reflect the pivotal role that the liver has in the homeostasis of many different bodily functions. In addition, they may have features related to the underlying cause of cirrhosis such as cryoglobulinemia from hepatitis C, diabetes mellitus and arthropathy in patients with hemochromatosis, or extrahepatic autoimmune diseases (such as hemolytic anemia or thyroiditis) in patients with autoimmune hepatitis.

Physical examination — A number of physical findings have been described in patients with cirrhosis, including jaundice, spider angiomata, gynecomastia, ascites, splenomegaly, palmar erythema, digital clubbing, and asterixis.

Decreasing blood pressure — As cirrhosis progresses, patients often have a decrease in mean arterial pressure [15]. Patients who were previously hypertensive may become normotensive or hypotensive. The decrease in mean arterial pressure contributes to the development of hepatorenal syndrome and is an important predictor of survival. (See "Hepatorenal syndrome", section on 'Pathogenesis' and "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Decompensated cirrhosis'.)

Skin findings — Patients with cirrhosis frequently develop jaundice and spider angiomata. Jaundice is a yellow coloring of the skin and mucous membranes that results from increased serum bilirubin. It is usually not detectable until the bilirubin is greater than 2 to 3 mg/dL. Hyperbilirubinemia may also cause the urine to appear dark or "cola" colored. (See "Diagnostic approach to the adult with jaundice or asymptomatic hyperbilirubinemia".)

Yellow discoloration to the skin can also be caused by excessive consumption of carotene (such as in patients who consume large quantities of carrots). Yellowing of the skin in carotenemia can be distinguished from jaundice by the absence of yellow discoloration in the sclera in the former.

Spider angiomata (also referred to as spider telangiectasias) are vascular lesions consisting of a central arteriole surrounded by many smaller vessels. They are most frequently found on the trunk, face, and upper limbs. The body of the lesion (the central arteriole) can be seen pulsating when compressed with a glass slide. Blood fills the central arteriole first before traveling to the peripheral tips of each "leg" after blanching. There are usually multiple radiating legs and surrounding erythema that may encompass the entire lesion or only its central portion.

The pathogenesis of spider angiomata is incompletely understood, but they are believed to result from alterations in sex hormone metabolism. One study suggested that the presence of spider angiomata in men was associated with an increase in the estradiol to free testosterone ratio [16]. Acquired spider angiomata are not specific for cirrhosis since they may also be seen during pregnancy (picture 1) and in patients with severe malnutrition.

They can also be seen in otherwise healthy people, who usually have fewer than three small lesions. As a general rule, the number and size of spider angiomata correlate with the severity of liver disease [17,18]. Patients with numerous, large spider angiomata may be at increased risk for variceal hemorrhage.

Head and neck findings — Head and neck findings in patients with cirrhosis may include parotid gland enlargement and fetor hepaticus. Parotid gland enlargement is typically seen in patients with alcoholic liver disease and is probably due to alcohol, not cirrhosis per se. Enlargement is usually secondary to fatty infiltration, fibrosis, and edema rather than a hyperfunctioning gland [19].

Fetor hepaticus refers to a sweet, pungent smell to the breath of a patient with cirrhosis. It is caused by increased concentrations of dimethyl sulfide, the presence of which suggests underlying severe portal-systemic shunting [20].

Chest findings — Gynecomastia is seen in up to two-thirds of patients with cirrhosis. It is possibly caused by increased production of androstenedione from the adrenals, enhanced aromatization of androstenedione to estrone, and increased conversion of estrone to estradiol [21]. Men may also develop other features reflecting feminization, such as loss of chest or axillary hair and inversion of the normal male pubic hair pattern. Gynecomastia can be seen in a variety of conditions other than cirrhosis. (See "Epidemiology, pathophysiology, and causes of gynecomastia".)

Gynecomastia is defined histologically as a benign proliferation of the glandular tissue of the male breast and is diagnosed on exam as a palpable mass of tissue (usually underlying the nipple). The evaluation of gynecomastia is discussed separately. (See "Clinical features, diagnosis, and evaluation of gynecomastia in adults".)

Abdominal findings — Findings on abdominal examination include hepatomegaly, splenomegaly, ascites, caput medusae, and a Cruveilhier-Baumgarten murmur.

Ascites — Ascites is the accumulation of fluid in the peritoneal cavity. Physical findings in patients with ascites include abdominal distension, a fluid wave, and flank dullness to percussion. The accuracy of physical findings is variable, depending in part on the amount of fluid present, the technique used to examine the patient, and the clinical setting (eg, detection may be more difficult in patients who are obese). In one study, the absence of flank dullness was the most accurate predictor against the presence of ascites; the probability of ascites being present was less than 10 percent in such patients [22]. However, approximately 1500 mL of fluid had to be present for flank dullness to be detected. (See "Evaluation of adults with ascites".)

Hepatomegaly — The cirrhotic liver may be enlarged, normal sized, or small. While the presence of a palpable liver may indicate liver disease, a non-palpable liver does not exclude

it. When palpable, the cirrhotic liver has a firm and nodular consistency. The liver is the largest internal organ in humans and typically spans 21 to 23 cm horizontally and 14 to 17 cm vertically. The size of the normal liver varies depending on sex, height, and body habitus.

Physical examination of the liver can be helpful for assessing its shape, its consistency, and whether there is tenderness of the liver edge. It is less useful for assessing its size since assessment of liver size by physical examination correlates poorly with radiologic assessment [23]. Nevertheless, the liver span can be estimated using percussion techniques or the scratch test. The scratch test uses auscultation while lightly scratching the skin. The intensity of the scratching sound increases when the liver is encountered with the scratching finger. A normal liver span in the mid-clavicular line by physical examination is 7 to 10 cm.

In healthy people, the liver is generally not palpable because it lies posterior to the rib cage. By contrast, an enlarged liver can often be palpated below the costal margin. However, there are exceptions in which a normal-sized liver can be palpated below the costal margin including patients with emphysema, a thin-body habitus, the presence of a hypertrophied caudate lobe (such as seen in patients with Budd-Chiari syndrome), or Riedel's lobe (an anatomical variant in which there is an extension of the right-lobe downward and lateral toward the gallbladder). (See "Overview of the evaluation of hepatomegaly in adults".)

Splenomegaly — Splenomegaly is common, especially in patients with cirrhosis from nonalcoholic etiologies [24]. It is believed to be caused primarily by congestion of the red pulp resulting from portal hypertension. However, splenic size does not correlate well with portal pressures, suggesting that other factors may be contributing [25]. The differential diagnosis of splenomegaly includes several other disorders. (See "Splenomegaly and other splenic disorders in adults".)

Caput medusae — The veins of the lower abdominal wall normally drain inferiorly into the iliofemoral system, while the veins of the upper abdominal wall drain superiorly into the veins of the thoracic wall and axilla. When portal hypertension occurs as the result of cirrhosis, the umbilical vein, normally obliterated in early life, may open. Blood from the portal venous system may be shunted through the periumbilical veins into the umbilical vein and ultimately to the abdominal wall veins, causing them to become prominent. This appearance has been said to resemble the head (caput) of the mythical Gorgon Medusa.

Dilated abdominal veins can also be seen in the inferior vena cava syndrome [26] and the superior vena cava syndrome (if obstruction includes the azygous system) [27]. In these conditions, collateral veins tend to be more prominent in the lateral aspect of the abdominal wall. One maneuver that has been proposed to distinguish vena caval obstruction from portal hypertension is to pass a finger along dilated veins located **below** the umbilicus to strip them of blood and determine the direction of blood flow during refilling. In portal-systemic collateral veins, the blood flow should be directed inferiorly, away from the

umbilicus, whereas vena caval collateral vein flow should be cephalad. However, the actual ability of this maneuver to discriminate between the two is poor, since in both conditions the dilated veins may lack valves and thus have bidirectional blood flow [28].

Cruveilhier-Baumgarten murmur — The Cruveilhier-Baumgarten murmur is a venous hum that may be auscultated in patients with portal hypertension. It results from collateral connections between the portal system and the remnant of the umbilical vein. It is best appreciated when the stethoscope is placed over the epigastrium. The murmur is augmented by maneuvers that increase intraabdominal pressure, such as the Valsalva maneuver, and diminished by applying pressure on the skin above the umbilicus [29].

Genitourinary findings — Men with cirrhosis may have testicular atrophy due to the development of hypogonadism. (See 'Symptoms' above.)

Extremity findings — Findings on examination of the extremities of a patient with cirrhosis may include palmar erythema, nail changes, clubbing, hypertrophic osteoarthropathy, and Dupuytren's contracture [30].

Palmar erythema is an exaggeration of the normal speckled mottling of the palm and is believed to be caused by altered sex hormone metabolism [25]. It is most frequently found on the thenar and hypothenar eminences, while sparing the central portions of the palm. Palmar erythema is not specific for liver disease and can be seen in association with pregnancy, rheumatoid arthritis, hyperthyroidism, and hematological malignancies.

Nail changes include Muehrcke nails and Terry nails. Muehrcke nails are paired horizontal white bands separated by normal color. The exact pathogenesis is unknown, but it is believed to be caused by hypoalbuminemia [31]. They are not specific for cirrhosis since they may also be seen in other conditions associated with a low serum albumin, such as the nephrotic syndrome. In patients with Terry nails, the proximal two-thirds of the nail plate appears white, whereas the distal one-third is red (picture 2). This finding is also believed to be secondary to a low serum albumin [31].

Clubbing and hypertrophic osteoarthropathy are two additional findings in patients with cirrhosis. Clubbing is present when the angle between the nail plate and proximal nail fold is greater than 180 degrees (figure 1). When severe, the distal finger has a "drum stick" appearance. Hypertrophic osteoarthropathy (HOA) is a chronic proliferative periostitis of the long bones that can cause considerable pain. Clubbing is more common in biliary causes of cirrhosis (particularly primary biliary cirrhosis), while hypertrophic osteoarthropathy can be seen with various causes of liver disease [32,33]. Neither feature is specific for liver disease. The pathogenesis of clubbing and hypertrophic osteoarthropathy is not well understood. The most frequent cause of hypertrophic osteoarthropathy is lung cancer, which should be

sought in the appropriate setting. (See "Overview of nail disorders", section on 'Clubbing' and "Malignancy and rheumatic disorders", section on 'Hypertrophic osteoarthropathy'.)

Dupuytren's contracture results from the thickening and shortening of the palmar fascia, which causes flexion deformities of the fingers (picture 3). Pathologically, it is characterized by fibroblastic proliferation and disorderly collagen deposition with fascial thickening. The pathogenesis is unknown but may be related to free radical formation generated by the oxidative metabolism of hypoxanthine [34]. It is relatively common in patients with alcoholic cirrhosis, in whom it may be found in as many as a third of patients [35]. However, it can also be seen in several other conditions, including in workers exposed to repetitive handling tasks or vibration, and patients with diabetes mellitus, reflex sympathetic dystrophy, cigarette smoking and alcohol consumption, and Peyronie's disease. (See "Dupuytren's contracture".)

Neurologic findings — Asterixis (bilateral but asynchronous flapping motions of outstretched, dorsiflexed hands) is seen in patients with hepatic encephalopathy. Asterixis may also be seen in patients with uremia and severe heart failure. (See "Hepatic encephalopathy in adults: Clinical manifestations and diagnosis".)

Laboratory findings — Several laboratory abnormalities may be seen in patients with cirrhosis. In addition, because it is common for panels of serum chemistries to be sent for screening or evaluation of specific complaints, laboratory abnormalities may be the first indication that a patient has cirrhosis. Common abnormalities include elevated serum bilirubin, abnormal aminotransferases, elevated alkaline phosphatase/gamma-glutamyl transpeptidase, a prolonged prothrombin time/elevated international normalized ratio (INR), hyponatremia, and thrombocytopenia. (See "Approach to the patient with abnormal liver tests".)

Liver function tests — Although the term "liver function tests" (LFTs) is commonly used, it is imprecise since many of the tests reflecting the health of the liver are not direct measures of its function. The most common laboratory measures classified as LFTs include the enzyme tests (principally the serum aminotransferases, alkaline phosphatase, and gamma-glutamyl transpeptidase), the serum bilirubin, and tests of synthetic function (principally the serum albumin concentration and prothrombin time).

- Aminotransferases – Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are usually moderately elevated in patients with cirrhosis. AST is more often elevated than ALT. However, normal aminotransferases do not preclude a diagnosis of cirrhosis [36]. Most forms of chronic hepatitis other than alcoholic liver disease have a ratio of AST/ALT less than one. However, as chronic hepatitis progresses to cirrhosis, the ratio of AST to ALT may reverse [37,38]. (See "Approach to the patient with abnormal liver tests", section on 'AST to ALT ratio'.)

- Alkaline phosphatase – Alkaline phosphatase is usually elevated in the setting of cirrhosis, but is less than two to three times the upper normal limit. Higher levels may be seen in patients with underlying cholestatic liver disease such as primary sclerosing cholangitis or primary biliary cirrhosis. (See "Enzymatic measures of hepatic cholestasis (alkaline phosphatase, 5'-nucleotidase, gamma-glutamyl transpeptidase)".)

- Gamma-glutamyl transpeptidase – Gamma-glutamyl transpeptidase (GGT) levels correlate reasonably well with alkaline phosphatase in liver disease but are nonspecific [39]. Levels of GGT are typically much higher in chronic liver disease from alcohol than other causes. This may be the result of alcohol-inducing hepatic microsomal GGT [40] or alcohol causing GGT to leak from hepatocytes [41]. (See "Enzymatic measures of hepatic cholestasis (alkaline phosphatase, 5'-nucleotidase, gamma-glutamyl transpeptidase)".)

- Bilirubin – Bilirubin levels may be normal in well-compensated cirrhosis. However, they rise as the cirrhosis progresses. In patients with primary biliary cirrhosis, a rising serum bilirubin portends a poor prognosis [42].

- Albumin – Albumin is synthesized exclusively in the liver. Albumin levels fall as the synthetic function of the liver declines with worsening cirrhosis. Thus, serum albumin levels can be used to help grade the severity of cirrhosis. Hypoalbuminemia is not specific for liver disease, since it may be seen in many other medical conditions such as heart failure, the nephrotic syndrome, protein losing enteropathy, or malnutrition. (See "Tests of the liver's biosynthetic capacity (eg, albumin, coagulation factors, prothrombin time)".)

- Prothrombin time – Most of the proteins involved in the coagulation process are produced in the liver. Thus, the prothrombin time reflects the degree of hepatic synthetic dysfunction. The prothrombin time increases as the ability of a cirrhotic liver to synthesize clotting factors diminishes. Thus, worsening coagulopathy correlates with the severity of hepatic dysfunction. (See "Tests of the liver's biosynthetic capacity (eg, albumin, coagulation factors, prothrombin time)".)

- Other liver function tests – The ability of the liver to transport organic anions and metabolize drugs has led to the development of a multitude of tests to assess the function of the liver. None is used routinely in clinical practice. (See "Tests of the liver's capacity to transport organic anions and metabolize drugs".)

Serum chemistries — Hyponatremia is common in patients with cirrhosis and ascites and is related to an inability to excrete free water. This results primarily from high levels of anti-diuretic hormone secretion [43]. Hyponatremia often becomes severe as cirrhosis progresses to end-stage liver disease [44]. (See "Hyponatremia in patients with cirrhosis".)

As cirrhosis progresses, patients may develop hepatorenal syndrome, with a progressive rise in serum creatinine. (See "Hepatorenal syndrome".)

Hematologic abnormalities — Patients with cirrhosis commonly have a number of hematologic abnormalities, including varying degrees of cytopenia. Thrombocytopenia is the most common hematologic abnormality, while leukopenia and anemia develop later in the disease course [45].

Thrombocytopenia is mainly caused by portal hypertension with attendant congestive splenomegaly. An enlarged spleen can result in temporary sequestration of up to 90 percent of the circulating platelet mass. However, this uncommonly results in platelet counts less than 50,000/mL, and unless complicated by coexisting coagulopathy, it is rarely a clinical problem [39]. Decreased thrombopoietin levels may also contribute to thrombocytopenia. (See "Clinical applications of thrombopoietic growth factors" and "Hemostatic abnormalities in patients with liver disease", section on 'Physiologic effects of hepatic dysfunction'.)

Anemia is usually multifactorial in origin; acute and chronic gastrointestinal blood loss, folate deficiency, direct toxicity due to alcohol, hypersplenism, bone marrow suppression (as in hepatitis-associated aplastic anemia), the anemia of chronic disease (inflammation), and hemolysis may all contribute. (See "Diagnostic approach to anemia in adults".)

Leukopenia and neutropenia are due to hypersplenism.

Other abnormalities — Globulins tend to be increased in patients with cirrhosis. This may be secondary to shunting of bacterial antigens in portal venous blood away from the liver to lymphoid tissue, which induces immunoglobulin production [46]. Marked elevations of IgG may be a clue to the presence of autoimmune hepatitis. Increased levels of IgM are present in 90 to 95 percent of patients with primary biliary cirrhosis.

In addition to deficiency of coagulant proteins, patients may develop varying degrees of disseminated intravascular coagulation, fibrinolysis, vitamin K deficiency, and dysfibrinogenemia, all of which may contribute to bleeding. (See "Hemostatic abnormalities in patients with liver disease".)

Patients often have laboratory findings related to diabetes mellitus. Diabetes mellitus is seen in 15 to 30 percent of patients with cirrhosis [47]. Insulin resistance is present in many patients with nonalcoholic fatty liver disease. Diabetes may also be common in patients with chronic hepatitis C. The pathogenesis is likely related to insulin resistance and an inadequate secretion of insulin from the beta cells of the pancreas [48]. Diabetes may also be seen in patients with hemochromatosis. (See "Extrahepatic manifestations of hepatitis C virus infection", section on 'Diabetes mellitus' and "Clinical features and diagnosis of metabolic dysfunction-associated steatotic liver disease (nonalcoholic fatty liver disease) in adults",

section on 'Risk factors and associated conditions' and "Clinical manifestations and diagnosis of hereditary hemochromatosis", section on 'Diabetes mellitus'.)

Radiologic findings — Radiologic studies such as abdominal ultrasound, computed tomography scan, and magnetic resonance imaging may suggest the presence of cirrhosis. Findings may include a liver that appears shrunken, irregular, and nodular. Imaging studies may also show evidence of varices and ascites in patients with portal hypertension. (See 'Imaging studies' below.)

DIAGNOSIS

In patients suspected of having cirrhosis, abdominal imaging (typically ultrasound) is obtained to evaluate the liver parenchyma and to detect extrahepatic manifestations of cirrhosis. A liver biopsy is required to definitively confirm the diagnosis. However, it is generally not necessary if the clinical, laboratory, and radiologic data strongly suggest the presence of cirrhosis and the results would not alter the patient's management. Noninvasive serologic and radiographic methods for diagnosing cirrhosis are also being developed. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations".)

When to suspect cirrhosis — Cirrhosis is often suspected in patients with [49]:

- Stigmata of chronic liver disease discovered on physical examination (table 1) (see 'Physical examination' above)
- Evidence of cirrhosis on laboratory or radiologic testing or by direct visualization while undergoing a surgical procedure
- Evidence of decompensated cirrhosis, which is characterized by the presence of dramatic and life-threatening complications, such as variceal hemorrhage, ascites, spontaneous bacterial peritonitis, or hepatic encephalopathy

A meta-analysis found that the factors with the best ability to predict cirrhosis in adults with known or suspected liver disease included [50]:

- Presence of ascites (likelihood ratio [LR] 7.2)
- Platelet count <160,000/mm^3 (LR 6.3)
- Spider angiomata (LR 4.3)
- Bonacini cirrhosis discriminant score greater than 7 (LR 9.4)

The Bonacini cirrhosis discriminant score is calculated by giving points for the following parameters [51]:

- Platelets (x1000/mm^3):
  - >340 – zero points
  - 280 to 339 – one point
  - 220 to 279 – two points
  - 160 to 219 – three points
  - 100 to 159 – four points
  - 40 to 99 – five points
  - <40 – six points
- Alanine aminotransferase to aspartate aminotransferase (ALT/AST) ratio:
  - >1.7 – zero points
  - 1.2 to 1.7 – one point
  - 0.6 to 1.19 – two points
  - <0.6 – three points
- International normalized ratio (INR):
  - <1.1 – zero points
  - 1.1 to 1.4 – one point
  - >1.4 – two points

Factors associated with a low likelihood of cirrhosis included:

- Lok index <20 percent (LR 0.09)
- Platelet count of 160,000/mm^3 or higher (LR 0.29)
- Absence of hepatomegaly (LR 0.37)

The Lok index is calculated using the platelet count, AST, ALT, and INR [52]. In a validation study, when a cutoff of <20 percent was used to exclude cirrhosis, the test had a specificity of 92 percent. When a cutoff of >50 percent was used to diagnose cirrhosis, the test had a sensitivity of 85 percent. Of note, the Lok index has only been validated in patients with hepatitis C virus.

Laboratory tests — Several noninvasive tests for the diagnosis of cirrhosis have been proposed, but none has yet emerged as a standard. Examples include the AST to platelet ratio index and FibroTest/FibroSure. Nevertheless, they can provide adjunctive information to conventional laboratory testing. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations".)

Imaging studies — Abdominal imaging is typically obtained in patients suspected of having cirrhosis, though radiographic imaging alone is not adequately sensitive or specific to diagnose cirrhosis. The findings must be viewed in light of other signs of cirrhosis, such as

physical examination or laboratory test findings. In addition to evaluating the liver, abdominal imaging may reveal hepatocellular carcinoma or extrahepatic findings suggestive of cirrhosis, such as ascites, varices, splenomegaly, and hepatic or portal vein thrombosis. Abdominal ultrasound is typically the first radiologic study obtained because it is readily available, provides information about the appearance of the liver and blood flow within the portal circulation, is less expensive than other imaging modalities, and does not expose patients to intravenous contrast or radiation.

In rare instances, radiographic findings suggest the etiology of cirrhosis. A hypertrophied caudate lobe discovered on computed tomographic (CT) scanning, for example, suggests Budd-Chiari syndrome [53]. Decreased signal intensity on magnetic resonance imaging may indicate iron overload from hereditary hemochromatosis (image 1) [54].

- **Ultrasonography** – Ultrasonography is routinely used during the evaluation of cirrhosis. It is noninvasive, well tolerated, widely available, and provides valuable information. In advanced cirrhosis, the liver may appear small and nodular. Surface nodularity and increased echogenicity with irregular appearing areas are consistent with cirrhosis, but can also be seen with hepatic steatosis [55,56]. There is typically atrophy of the right lobe and hypertrophy of the caudate or left lobes. Investigators have attempted to use the ratio of the width of the caudate lobe to the width of the right lobe as an ultrasonographic criterion for the diagnosis of cirrhosis. However, the sensitivity is poor [57].

  In one study of high-resolution ultrasonography in patients suspected of having cirrhosis who underwent liver biopsy, ultrasonography had a sensitivity of 91 percent and a specificity of 94 percent for making the diagnosis [58].

  Ultrasonography may also be used as a screening test for hepatocellular carcinoma and portal hypertension. The finding of nodules on ultrasonography warrants further evaluation since benign and malignant nodules can have similar ultrasonographic appearances. Findings of portal hypertension include an increased diameter of the portal vein, the presence of collateral veins, and decreased flow within the portal circulation on Doppler imaging [2,59]. Ultrasonography is also useful for detecting splenomegaly, ascites, and portal vein thrombosis.

- **Computed tomography** – CT is not routinely used in the diagnosis and evaluation of cirrhosis. It provides similar information to ultrasonography, but at the expense of radiation and contrast exposure. CT findings of hepatic nodularity, atrophy of the right lobe and hypertrophy of the caudate or left lobes, ascites, or varices suggest the presence of cirrhosis, but they are not diagnostic. Patency of the portal vein can be demonstrated with CT portal phase imaging, but the direction of blood flow cannot be determined.

- **Magnetic resonance imaging** – The role of magnetic resonance imaging (MRI) in the diagnosis of cirrhosis is unclear. Despite much enthusiasm about the potential of MRI in the evaluation of patients with cirrhosis, its use is limited by expense, poor tolerance of the examination by some patients, and the ability to obtain information provided by MRI through other means.

  Some authors report that MRI can accurately diagnose cirrhosis and provide correlation with its severity [60-62]. One study found the sensitivity and specificity of an MRI scoring system in distinguishing Child-Pugh grade A cirrhosis from other grades to be 93 and 82 percent, respectively [60]. MRI may also reveal iron overload and provide an estimate of the hepatic iron concentration [54,63,64]. Magnetic resonance angiography (MRA) is more sensitive than ultrasonography for diagnosing complications of cirrhosis, such as portal vein thrombosis [65]. Unlike CT portal phase imaging, MRA can determine the volume and direction of blood flow in the portal vein.

- **Elastography** – Increasing scarring of the liver is associated with increasing "stiffness" of the tissue. Several methods have been developed to assess liver stiffness. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations", section on 'Imaging examinations'.)

- **Nuclear studies** – Radionuclide testing can be useful in suggesting the diagnosis of cirrhosis [66]. 99mTc sulfur colloid is normally taken up by cells of the reticuloendothelial system. In patients with cirrhosis, there may be heterogeneity in the uptake of 99mTc sulfur colloid by the liver and increased uptake by the spleen and bone marrow. The exact sensitivity and specificity of these findings in making the diagnosis of cirrhosis is unknown. Given the widespread use of other imaging modalities, this test is seldom performed in clinical practice.

Liver biopsy — The gold standard for diagnosing cirrhosis is examination of an explanted liver, either at autopsy or following liver transplantation, because the architecture of the entire liver can be appreciated. In clinical practice, cirrhosis is diagnosed with a liver biopsy (picture 4), during which a sample of the liver is obtained by either a percutaneous, transjugular, laparoscopic, or radiographically-guided fine-needle approach. The method for obtaining the biopsy will depend on the clinical setting [67]. The sensitivity of a liver biopsy for cirrhosis is in the range of 80 to 100 percent, depending on the method used, and the size and number of specimens obtained. (See "Approach to liver biopsy" and "Transjugular liver biopsy".)

However, liver biopsy is not necessary if the clinical, laboratory, and radiologic data strongly suggest the presence of cirrhosis and if the results would not alter the patient's management. An example would be a patient with a history of heavy alcohol use who has ascites, severe coagulopathy, and a shrunken, nodular-appearing liver on ultrasonography.

In addition to demonstrating that cirrhosis is present, a liver biopsy can sometimes suggest the cause. This is especially true for metabolic causes of cirrhosis such as hereditary hemochromatosis (picture 5), nonalcoholic steatohepatitis (picture 6), Wilson disease (picture 7), and alpha-1 antitrypsin deficiency. (See "Approach to the patient with suspected iron overload", section on 'Liver biopsy' and "Wilson disease: Clinical manifestations, diagnosis, and natural history", section on 'Diagnostic evaluation' and "Clinical features and diagnosis of metabolic dysfunction-associated steatotic liver disease (nonalcoholic fatty liver disease) in adults".)

Investigational tests — Preliminary studies have suggested that artificial intelligence shows promise as a diagnostic tool by identifying cirrhosis-related electrocardiogram (ECG) abnormalities. In a study comparing ECG findings in over 5000 patients with decompensated cirrhosis, with an age- and sex-matched control group, an artificial intelligence model using ECG criteria distinguished cirrhosis from no cirrhosis with a sensitivity and specificity of 85 and 83 percent, respectively [68].

DETERMINING THE CAUSE OF CIRRHOSIS

Many causes of chronic liver injury can lead to cirrhosis (table 2), and a specific etiology can be determined in 85 to 90 percent of patients [69]. Determining the etiology of cirrhosis is important because it may influence treatment decisions, permit counseling of family members, and help predict the patient's prognosis. The initial evaluation includes obtaining a history, performing a physical examination, and obtaining routine blood tests (ie, liver biochemical and function tests and a complete blood count). The findings from the initial evaluation are then used to guide additional testing. (See "Approach to the patient with abnormal liver tests", section on 'Initial evaluation'.)

If the initial evaluation does not help guide the evaluation (eg, in a patient with an unremarkable history and normal laboratory tests), testing for common causes of cirrhosis should be performed. An overview of the approach to determining the cause of a patient's liver disease is discussed in detail elsewhere. In addition, detailed discussions of the diagnosis of specific disorders can be found in their respective topic reviews. (See 'Etiologies and classification' above and "Approach to the patient with abnormal liver tests".)

WHEN TO REFER TO A SPECIALIST

Referral to a hepatologist should be considered in patients suspected of having cirrhosis if the diagnosis remains unclear after noninvasive testing (eg, imaging and laboratory tests). In particular, referral should be considered prior to obtaining a liver biopsy. It is also reasonable to refer to a specialist to aid with determining the cause of the cirrhosis if common etiologies

are ruled out (eg, hepatitis C) or to aid with management. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'When to refer to a specialist'.)

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: Cirrhosis".)

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 topics (see "Patient education: Cirrhosis (The Basics)")
- Beyond the Basics topics (see "Patient education: Cirrhosis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Etiology** – There are numerous causes of liver disease that can result in cirrhosis, either by causing chronic hepatic inflammation or cholestasis (table 2). (See 'Etiologies and classification' above.)

  Determining the etiology of cirrhosis is important because it may influence treatment decisions, permit counseling of family members, and help predict the patient's prognosis. The initial evaluation includes obtaining a history, performing a physical examination, and obtaining routine blood tests (ie, liver biochemical and function tests and a complete blood count). The findings from the initial evaluation are then used to

guide additional testing. (See "Approach to the patient with abnormal liver tests", section on 'Initial evaluation'.)

- **Clinical manifestations** – The clinical manifestations of cirrhosis may include nonspecific symptoms (eg, anorexia, weight loss, weakness, fatigue) or signs and symptoms of hepatic decompensation (jaundice, pruritus, signs of upper gastrointestinal bleeding, abdominal distension from ascites, confusion due to hepatic encephalopathy) (table 1). Physical examination findings may include jaundice, spider angiomata, gynecomastia, ascites, splenomegaly, palmar erythema, digital clubbing, and asterixis. Laboratory abnormalities may include elevated serum bilirubin, abnormal aminotransferases, elevated alkaline phosphatase/gamma-glutamyl transpeptidase, a prolonged prothrombin time/elevated international normalized ratio (INR), hyponatremia, and thrombocytopenia. (See 'Laboratory findings' above.)

- **When to suspect cirrhosis** – Cirrhosis is often suspected in patients with (see 'When to suspect cirrhosis' above):

  - Stigmata of chronic liver disease discovered on physical examination (see 'Physical examination' above)

  - Evidence of cirrhosis on laboratory or radiologic testing or by direct visualization while undergoing a surgical procedure

  - Evidence of decompensated cirrhosis, which is characterized by the presence of dramatic and life-threatening complications such as variceal hemorrhage, ascites, spontaneous bacterial peritonitis, or hepatic encephalopathy

- **Radiographic imaging** – In patients suspected of having cirrhosis, abdominal imaging is typically obtained, though radiographic imaging alone is not adequately sensitive or specific to diagnose cirrhosis. The findings must be viewed in light of other signs of cirrhosis such as physical examination or laboratory test findings. In addition to evaluating the liver, abdominal imaging may reveal hepatocellular carcinoma or extrahepatic findings suggestive of cirrhosis such as ascites, varices, splenomegaly, and hepatic or portal vein thrombosis. (See 'Imaging studies' above.)

  Abdominal ultrasound is typically the first radiologic study obtained because it is readily available, provides information about the appearance of the liver and blood flow within the portal circulation, is less expensive than other imaging modalities, and does not expose patients to intravenous contrast or radiation.

- **Methods for establishing the diagnosis** – Noninvasive serologic and radiographic methods for establishing the cirrhosis are being developed and are discussed in detail

separately. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations".)

A liver biopsy can be performed to definitively confirm the diagnosis of cirrhosis. However, it is generally not necessary if the clinical, laboratory, and radiologic data strongly suggest the presence of cirrhosis and the results would not alter the patient's management. (See 'Liver biopsy' above.)

REFERENCES

1. Wong RJ, Aguilar M, Cheung R, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterology 2015; 148:547.
2. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician 2006; 74:756.
3. Anthony PP, Ishak KG, Nayak NC, et al. The morphology of cirrhosis. Recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. J Clin Pathol 1978; 31:395.
4. Fauerholdt L, Schlichting P, Christensen E, et al. Conversion of micronodular cirrhosis into macronodular cirrhosis. Hepatology 1983; 3:928.
5. Van de Water J, Cooper A, Surh CD, et al. Detection of autoantibodies to recombinant mitochondrial proteins in patients with primary biliary cirrhosis. N Engl J Med 1989; 320:1377.
6. Abrams GA, Concato J, Fallon MB. Muscle cramps in patients with cirrhosis. Am J Gastroenterol 1996; 91:1363.
7. Baskol M, Ozbakir O, Coşkun R, et al. The role of serum zinc and other factors on the prevalence of muscle cramps in non-alcoholic cirrhotic patients. J Clin Gastroenterol 2004; 38:524.
8. Angeli P, Albino G, Carraro P, et al. Cirrhosis and muscle cramps: evidence of a causal relationship. Hepatology 1996; 23:264.
9. Konikoff F, Theodor E. Painful muscle cramps. A symptom of liver cirrhosis? J Clin Gastroenterol 1986; 8:669.
10. Mehta SS, Fallon MB. Muscle cramps in liver disease. Clin Gastroenterol Hepatol 2013; 11:1385.
11. Kalaitzakis E. Gastrointestinal dysfunction in liver cirrhosis. World J Gastroenterol 2014; 20:14686.
12. Burra P, Germani G, Masier A, et al. Sexual dysfunction in chronic liver disease: is liver transplantation an effective cure? Transplantation 2010; 89:1425.

13. Cundy TF, Butler J, Pope RM, et al. Amenorrhoea in women with non-alcoholic chronic liver disease. Gut 1991; 32:202.
14. van Thiel DH, Gavaler JS, Spero JA, et al. Patterns of hypothalamic-pituitary-gonadal dysfunction in men with liver disease due to differing etiologies. Hepatology 1981; 1:39.
15. Ge PS, Runyon BA. The changing role of beta-blocker therapy in patients with cirrhosis. J Hepatol 2014; 60:643.
16. Pirovino M, Linder R, Boss C, et al. Cutaneous spider nevi in liver cirrhosis: capillary microscopical and hormonal investigations. Klin Wochenschr 1988; 66:298.
17. Zaman A, Hapke R, Flora K, et al. Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol 1999; 94:3292.
18. Foutch PG, Sullivan JA, Gaines JA, Sanowski RA. Cutaneous vascular spiders in cirrhotic patients: correlation with hemorrhage from esophageal varices. Am J Gastroenterol 1988; 83:723.
19. Dutta SK, Dukehart M, Narang A, Latham PS. Functional and structural changes in parotid glands of alcoholic cirrhotic patients. Gastroenterology 1989; 96:510.
20. Tangerman A, Meuwese-Arends MT, Jansen JB. Cause and composition of foetor hepaticus. Lancet 1994; 343:483.
21. Van Thiel DH, Gavaler JS, Schade RR. Liver disease and the hypothalamic pituitary gonadal axis. Semin Liver Dis 1985; 5:35.
22. 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.
23. Niederau C, Sonnenberg A, Müller JE, et al. Sonographic measurements of the normal liver, spleen, pancreas, and portal vein. Radiology 1983; 149:537.
24. Soper NJ, Rikkers LF. Effect of operations for variceal hemorrhage on hypersplenism. Am J Surg 1982; 144:700.
25. Erlinger S, Benhamou J. Cirrhosis: Clinical aspects. In: Oxford Textbook of Clinical Hepatology, Mcintyre N, Benhamou J, Rizzetto M, et al (Eds), University Press, Oxford 1991. p.380.
26. MISSAL ME, ROBINSON JA, TATUM RW. INFERIOR VENA CAVA OBSTRUCTION: CLINICAL MANIFESTATIONS, DIAGNOSTIC METHODS, AND RELATED PROBLEMS. Ann Intern Med 1965; 62:133.
27. Nieto AF, Doty DB. Superior vena cava obstruction: clinical syndrome, etiology, and treatment. Curr Probl Cancer 1986; 10:441.
28. Coetzee T. Clinical anatomy of the umbilicus. S Afr Med J 1980; 57:463.
29. Groszmann R, Franchis R. Portal Hypertension. In: Diseases of the Liver, Eighth Edition, Schiff E, Sorrell M, Maddrey W (Eds), Lippincott Williams & Wilkens, Philadelphia 1999. p.4

15.

30. Sharma B, John S.. StatPearls, StatPearls Publishing, Treasure Island (FL) 2020.
31. Fitzpatrick T, Johnson R, Polano M, et al. Color Atlas and Synopsis of Clinical Dermatology: Common and Serious Diseases, Second edition, McGraw Hill, Inc, New York 1994.
32. Mills PR, Vallance R, Birnie G, et al. A prospective survey of radiological bone and joint changes in primary biliary cirrhosis. Clin Radiol 1981; 32:297.
33. Epstein O, Dick R, Sherlock S. Prospective study of periostitis and finger clubbing in primary biliary cirrhosis and other forms of chronic liver disease. Gut 1981; 22:203.
34. Murrell GA, Francis MJ, Bromley L. Free radicals and Dupuytren's contracture. Br Med J (Clin Res Ed) 1987; 295:1373.
35. Attali P, Ink O, Pelletier G, et al. Dupuytren's contracture, alcohol consumption, and chronic liver disease. Arch Intern Med 1987; 147:1065.
36. Ellis G, Goldberg DM, Spooner RJ, Ward AM. Serum enzyme tests in diseases of the liver and biliary tree. Am J Clin Pathol 1978; 70:248.
37. Sheth SG, Flamm SL, Gordon FD, Chopra S. AST/ALT ratio predicts cirrhosis in patients with chronic hepatitis C virus infection. Am J Gastroenterol 1998; 93:44.
38. Williams AL, Hoofnagle JH. Ratio of serum aspartate to alanine aminotransferase in chronic hepatitis. Relationship to cirrhosis. Gastroenterology 1988; 95:734.
39. Pratt D, Kaplan M. Evaluation of the Liver A: Laboratory Tests. In: Schiff's Diseases of the Liver, Eighth Edition, Schiff E, Sorrell M, Maddrey W (Eds), Lippincott Williams & Wilkens, Philadelphia 1999. p.205.
40. Goldberg DM. Structural, functional, and clinical aspects of gamma-glutamyltransferase. CRC Crit Rev Clin Lab Sci 1980; 12:1.
41. Barouki R, Chobert MN, Finidori J, et al. Ethanol effects in a rat hepatoma cell line: induction of gamma-glutamyltransferase. Hepatology 1983; 3:323.
42. Krzeski P, Zych W, Kraszewska E, et al. Is serum bilirubin concentration the only valid prognostic marker in primary biliary cirrhosis? Hepatology 1999; 30:865.
43. Asbert M, Ginès A, Ginès P, et al. Circulating levels of endothelin in cirrhosis. Gastroenterology 1993; 104:1485.
44. Papadakis MA, Fraser CL, Arieff AI. Hyponatraemia in patients with cirrhosis. Q J Med 1990; 76:675.
45. Qamar AA, Grace ND, Groszmann RJ, et al. Incidence, prevalence, and clinical significance of abnormal hematologic indices in compensated cirrhosis. Clin Gastroenterol Hepatol 2009; 7:689.
46. Triger DR, Wright R. Hyperglobulinaemia in liver disease. Lancet 1973; 1:1494.

47. Bianchi G, Marchesini G, Zoli M, et al. Prognostic significance of diabetes in patients with cirrhosis. Hepatology 1994; 20:119.
48. Petrides AS, Vogt C, Schulze-Berge D, et al. Pathogenesis of glucose intolerance and diabetes mellitus in cirrhosis. Hepatology 1994; 19:616.
49. Runyon BA. A Primer on Detecting Cirrhosis and Caring for These Patients without Causing Harm. Int J Hepatol 2011; 2011:801983.
50. Udell JA, Wang CS, Tinmouth J, et al. Does this patient with liver disease have cirrhosis? JAMA 2012; 307:832.
51. Bonacini M, Hadi G, Govindarajan S, Lindsay KL. Utility of a discriminant score for diagnosing advanced fibrosis or cirrhosis in patients with chronic hepatitis C virus infection. Am J Gastroenterol 1997; 92:1302.
52. Lok AS, Ghany MG, Goodman ZD, et al. Predicting cirrhosis in patients with hepatitis C based on standard laboratory tests: results of the HALT-C cohort. Hepatology 2005; 42:282.
53. Becker CD, Scheidegger J, Marincek B. Hepatic vein occlusion: morphologic features on computed tomography and ultrasonography. Gastrointest Radiol 1986; 11:305.
54. Ernst O, Sergent G, Bonvarlet P, et al. Hepatic iron overload: diagnosis and quantification with MR imaging. AJR Am J Roentgenol 1997; 168:1205.
55. Di Lelio A, Cestari C, Lomazzi A, Beretta L. Cirrhosis: diagnosis with sonographic study of the liver surface. Radiology 1989; 172:389.
56. Sanford NL, Walsh P, Matis C, et al. Is ultrasonography useful in the assessment of diffuse parenchymal liver disease? Gastroenterology 1985; 89:186.
57. Giorgio A, Amoroso P, Lettieri G, et al. Cirrhosis: value of caudate to right lobe ratio in diagnosis with US. Radiology 1986; 161:443.
58. Simonovský V. The diagnosis of cirrhosis by high resolution ultrasound of the liver surface. Br J Radiol 1999; 72:29.
59. Zwiebel WJ. Sonographic diagnosis of hepatic vascular disorders. Semin Ultrasound CT MR 1995; 16:34.
60. Ito K, Mitchell DG, Hann HW, et al. Viral-induced cirrhosis: grading of severity using MR imaging. AJR Am J Roentgenol 1999; 173:591.
61. Ito K, Mitchell DG, Gabata T, Hussain SM. Expanded gallbladder fossa: simple MR imaging sign of cirrhosis. Radiology 1999; 211:723.
62. Ito K, Mitchell DG, Hann HW, et al. Progressive viral-induced cirrhosis: serial MR imaging findings and clinical correlation. Radiology 1998; 207:729.
63. Bonkovsky HL, Rubin RB, Cable EE, et al. Hepatic iron concentration: noninvasive estimation by means of MR imaging techniques. Radiology 1999; 212:227.

64. Gandon Y, Guyader D, Heautot JF, et al. Hemochromatosis: diagnosis and quantification of liver iron with gradient-echo MR imaging. Radiology 1994; 193:533.
65. Finn JP, Kane RA, Edelman RR, et al. Imaging of the portal venous system in patients with cirrhosis: MR angiography vs duplex Doppler sonography. AJR Am J Roentgenol 1993; 161:989.
66. McLaren MI, Fleming JS, Walmsley BH, et al. Dynamic liver scanning in cirrhosis. Br J Surg 1985; 72:394.
67. Bravo AA, Sheth SG, Chopra S. Liver biopsy. N Engl J Med 2001; 344:495.
68. Ahn JC, Attia ZI, Rattan P, et al. Development of the AI-Cirrhosis-ECG Score: An Electrocardiogram-Based Deep Learning Model in Cirrhosis. Am J Gastroenterol 2022; 117:424.
69. Charlton MR, Kondo M, Roberts SK, et al. Liver transplantation for cryptogenic cirrhosis. Liver Transpl Surg 1997; 3:359.

Topic 1253 Version 38.0

Contributor Disclosures

Eric Goldberg, MD No relevant financial relationship(s) with ineligible companies to disclose. **Sanjiv Chopra, MD, MACP** No relevant financial relationship(s) with ineligible companies to disclose. **Bruce A Runyon, MD, FAASLD** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy