Cirrhosis

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KEYWORDS

• Cirrhosis • Liver • Ascites • Jaundice • Encephalopathy • Edema
• Physical examination • Spider nevi

KEY POINTS

- Cirrhosis is a chronic condition that develops over many years and results in a myriad of physical examination findings.
- Many signs and symptoms associated with liver disease are nonspecific, but some findings, such as dilated abdominal veins, ascites, encephalopathy, abnormal hair distribution, and gynecomastia, are more specific and suggest underlying cirrhosis.
- Early identification of physical findings that suggest cirrhosis can guide the clinician to order testing aimed at determining the underlying cause of cirrhosis, provide lifestyle counseling to avoid progression of disease, and suggest appropriate treatment and screening recommendations.

INTRODUCTION

Cirrhosis is a chronic condition resulting from inflammation and fibrosis of the liver. Fibrosis leads to distortion of the normal architecture of the liver and formation of nodules.[1] This process happens slowly, typically over decades, and leads to changes in blood flow through the liver as well as disruption of normal hepatocellular function. The gold standard for diagnosing cirrhosis is liver biopsy. Previously, cirrhosis was thought to be irreversible; however, recent evidence supports the idea that advanced fibrosis and even cirrhosis can be reversible with treatment of the underlying cause.[2] Although mortality rates for cirrhosis and hepatocellular carcinoma from all causes had been increasing in the United States between 2007 and 2016, mortality rates significantly declined for hepatitis C–related cirrhosis starting in 2014 due to the availability of direct-acting antiviral therapy.[3]

Author contributions: All authors contributed to drafting and critical revision of the article.
Conflict of Interest Disclosure: D.M. Williams's spouse is a co-founder and co-owner of Certus Critical Care, Inc, a medical device company. They currently have no devices on the market. R. Wilson reports no conflict of interest.
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Med Clin N Am 106 (2022) 437–446
https://doi.org/10.1016/j.mcna.2021.12.001
0025-7125/22/

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The most common causes of cirrhosis in the United States include alcoholic liver disease, viral hepatitis, and nonalcoholic fatty liver disease.[4] Other, less common causes include autoimmune hepatitis, primary biliary cholangitis, cardiac cirrhosis, hemochromatosis, Wilson disease, cryptogenic cirrhosis, and others. Regardless of the cause, the complications of cirrhosis are similar and include bleeding due to decreased clotting factors; sequelae of increased portal pressure including esophageal varices and ascites; thrombocytopenia due to splenic sequestration; and decreased production of thrombopoietin, hepatic encephalopathy, infection, and renal failure.

In the clinical setting, patients are often categorized as having compensated or decompensated cirrhosis based on symptoms. Patients with compensated disease may present without any symptoms, whereas decompensated cirrhosis is often marked by variceal bleeding, ascites, or hepatic encephalopathy. The rate of transition from compensated to decompensated cirrhosis has been noted to be 4% to 10% per year, with an associated significant increase in mortality.[5]

Patients with cirrhosis may have a myriad of physical examination findings that reflect the severity of the underlying liver disease.[1] Although many signs and symptoms related to cirrhosis are nonspecific, such as abdominal pain, nausea, and malaise, some findings are more specific and point to complications of liver disease. In the next section, the authors discuss common physical examination maneuvers and findings that are relevant in cirrhosis. Where possible, likelihood ratios (LR) will be used to measure the utility of the examination maneuver or physical finding in the diagnosis of cirrhosis. Likelihood ratios are diagnostic weights that help clinicians interpret the physical examination findings of individual patients. Positive likelihood ratios greater than 1 increase the probability that the patient has the disease in question, where higher numbers denote increased significance. Negative likelihood ratios less than 1 decrease the probability that the patient has the disease in question, where lower numbers denote increased significance and thereby help to rule out a particular disease being looked for.[6]

HEPATOMEGALY AND THE LIVER EXAMINATION

When considering the diagnosis of cirrhosis, the abdominal examination, specifically the liver examination, plays an important role. There are 2 main methods for evaluating liver size at the midclavicular line (MCL). One method uses percussion alone, whereas another uses percussion on the superior aspect of the liver border and palpation or percussion on the inferior aspect. Although livers vary in size and shape based on gender and body habitus, it is expected that liver size less than 12 to 13 cm at the MCL rules out hepatomegaly.[7] Although occasionally used in clinical practice, newer studies suggest that the “scratch method” is subpar to palpation and percussion and should not be used when evaluating the liver.[8]

If the liver is palpable, this does not necessarily indicate enlarged liver size but does increase the likelihood of hepatomegaly. Conversely, the probability of hepatomegaly is reduced if a liver is nonpalpable.[7] When evaluating patients with chronic liver disease for the presence of cirrhosis, the positive likelihood ratio is 2.3 if hepatomegaly is present, with a negative likelihood ratio of 0.6 if hepatomegaly is not observed.[9]

Multiple other physical examination maneuvers investigating the liver can be performed to aid in the diagnosis of cirrhosis. The examination with the highest likelihood ratio to indicate cirrhosis is a firm liver edge on palpation, which has a positive likelihood ratio of 3.3.[9] Other findings, such as a palpable liver in the epigastrium, can also be helpful in the diagnosis of cirrhosis. As the liver changes, the left lobe atrophies

when compared with the right lobe, and the liver is more easily palpated as the tissue becomes more firm. Patients with cirrhosis also have alterations in their body habitus, leading to wasting of abdominal musculature, which allows for easier palpation.[10] If the liver is palpable in the epigastrium, the likelihood ratio for cirrhosis is 2.7. Conversely, if it is not palpated in the epigastrium, the chance of cirrhosis decreases, as the negative likelihood ratio is 0.3.[9]

SPLENOMEGALY

Splenomegaly can be found in patients with hematological disorders, infectious diseases, or hepatic diseases. In a small subset of patients (3%–12%), splenomegaly can be a normal variant.[11] Examination of the spleen is challenging, however can be quite useful when splenomegaly is identified. Splenomegaly is defined as a spleen that is 13 cm or greater in cephalocaudal diameter as identified by ultrasound.[11] Most of the available data support the use of percussion and palpation for the detection of splenomegaly on physical examination, although confirmation with ultrasound is usually required.

There are 3 main percussion techniques used to examine the spleen: percussion via the Nixon method, percussion via the Castell method, and percussion of the Traube space.[11] Although all 3 of these techniques have been validated by ultrasound to confirm validity in detecting splenomegaly, the Nixon method and percussion of Traube space are slightly more reliable. In the evaluation of splenomegaly, the Castell method has a positive LR of 1.7, the Nixon method has a positive LR of 2.0, and Traube space dullness has a positive LR of 2.1.[12]

Evaluation of the spleen via palpation may have higher accuracy than percussion. There are 3 main techniques used to evaluate spleen size via palpation: two-handed palpation with the patient in the right lateral decubitus position, one-handed palpation with the patient supine, and the hooking maneuver of Middleton with patient supine. The supine one-handed palpation has the most data to support this method.[11] If the spleen is palpable by any technique, the positive LR of having splenomegaly is 8.5.[12] By performing both percussion and palpation together, the detection of splenomegaly is more likely.

In addition to the finding of splenomegaly, other examination findings aid in identification of underlying pathology. If a patient has both splenomegaly and lymphadenopathy, underlying hepatic disease is less likely (LR of 0.04).[12] In patients with cirrhosis, the associated portal hypertension leads to increased portal venous pressure gradient with resultant splenomegaly.[13] The probability of cirrhosis in patients with underlying liver disease and splenomegaly has a positive LR of 2.5 and negative LR of 0.8.[9]

JAUNDICE

Jaundice refers to yellow discoloration of the skin, which occurs due to pigment buildup, most commonly bilirubin. Although bilirubin can stain all tissue, jaundice is typically most prominent in the face, mucosal membranes, trunk, and conjunctiva (**Fig. 1**). It is typically not visible unless serum bilirubin levels are at least 3 mg/dL or higher. When considering causes of jaundice other than hepatic dysfunction, it is important to note whether the discoloration is evenly distributed throughout the conjunctiva, as other causes of yellow discoloration (such as carotenemia) are not uniform across the sclera and skin.[14] Jaundice in the setting of chronic liver disease has a positive likelihood ratio of 3.8 supporting the diagnosis of cirrhosis, whereas the negative likelihood is 0.8.[9]

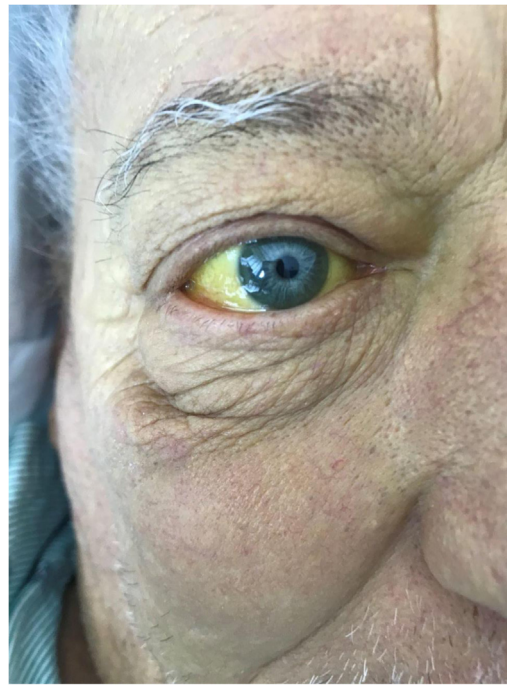

Fig. 1. Scleral icterus and jaundice of the skin. (Image courtesy of Paul Aronowitz, MD, Sacramento, CA.)

ASCITES

If a patient reports abdominal distention or increasing girth, it is important to identify the underlying cause. It may be due to feces, gas within the bowel, pregnancy, abdominal mass, fat, or fluid. Pathologic fluid accumulation in the abdomen is known as ascites. Over time, cirrhosis can progress to the development of portal hypertension, salt and fluid retention, and subsequent accumulation of ascites. A diagnostic paracentesis with calculation of the serum to ascites albumin gradient aids in identifying the underlying pathology that led to ascites. Eighty-four percent of cases of ascites are due to cirrhosis.[15] Other causes include pancreatitis, nephrotic syndrome, cardiac ascites, peritoneal carcinomatosis, infections (especially peritoneal tuberculosis), massive hepatic metastasis, and other rare causes.

History and physical examination are helpful in determining the presence of ascites. Typically, at least 1500 mL of fluid must be present in the abdomen in order to be detected by physical examination. Therefore, a clinician's inability to detect fluid on examination does not reliably exclude the diagnosis.[16] The gold standard for diagnosis of ascites is ultrasound, as it can detect volumes as small as 100 mL.[15]

The 4 main examination findings that suggest underlying ascites include fluid wave, bulging flanks, flank dullness, and shifting dullness. If present, the fluid wave has the highest positive likelihood ratio of 5.0. Shifting dullness follows this with a positive likelihood ratio of 2.3. Although these maneuvers are specific to the abdomen, it is important to examine the patient as a whole. If edema is detected on examination in addition to abdominal distention, the likelihood ratio of having underlying ascites is 3.8.[12]

When assessing for ascites, the lack of certain examination findings can be just as helpful as the presence of others. The absence of edema in the setting of abdominal distension decreases the probability of ascites with a negative likelihood ratio of 0.2. Flank tympany (or absence of flank fullness) has a negative LR of 0.3. The absence of bulging flanks and/or shifting dullness both decrease the probability of ascites with a negative likelihood ratio of 0.4.[12]

Diagnosing ascites and determining the underlying pathology is critical for patient care. Examination findings help guide the clinician to the diagnosis of ascites, increase clinical suspicion for spontaneous bacterial peritonitis (SBP), and suggest the need for timely paracentesis in order to guide patient care. SBP is a hallmark complication of ascites in which the fluid becomes infected; this is relatively common and can be deadly if left untreated or if treatment is delayed.

ENCEPHALOPATHY

In the setting of cirrhosis, vascular shunting and decreased liver mass can result in the accumulation of gut-derived neurotoxins in the body.[1] This build-up leads to encephalopathy, which can progress to coma if left untreated. Other conditions also present with encephalopathy without the presence of underlying cirrhosis, including hypertensive emergency, uremia, toxic ingestions, and others.

The physical examination is crucial for making the diagnosis of encephalopathy. Families may notice changes in patients' personalities, decreased mental sharpness, or disruption of the sleep-wake cycle, which often prompts presentation to a health care provider. On examination, the patient's mental status can vary from somnolent to agitated. If the patient is alert enough to participate in an examination, outstretched arms with wrist extension can produce asterixis, which is also known as a "flap." Clinicians pair these findings to make the clinical diagnosis of encephalopathy.

If encephalopathy is present in patients with chronic liver disease, the likelihood ratio for underlying cirrhosis is 8.8.[9] If hepatic encephalopathy is present, it is critical to look for the underlying trigger of this decompensation. Infections, electrolyte derangements, infections such as SBP, and gastrointestinal bleeding are common inciting events for hepatic encephalopathy.[1] Of note, although serum ammonia levels are found to be elevated in hepatic encephalopathy, the levels do not correspond to the severity of the underlying disease and cannot be monitored to assess for disease progression or improvement.

DILATED ABDOMINAL VEINS

Abdominal wall veins become dilated when venous obstruction is present and collateral blood flow subsequently develops. Most commonly, this is due to portal hypertension, but it can be due to other causes such as thrombosis, extrinsic compression of the superior or inferior vena cava, and other less common causes. By examining the direction of the blood flow within the dilated vessels, a clinician can distinguish between potential etiologies.[14] The examiner must evaluate the blood flow both in cranial to umbilicus and caudal to umbilicus directions.[13] If portal hypertension is the underlying cause, the blood will flow away from the umbilicus in cranial and caudal directions.

Cirrhosis is one of the primary causes of portal hypertension with subsequent abdominal vein dilation. This dilation can result in a venous rosette around the umbilicus, termed caput medusae. If a caput medusae is present in patients with underlying liver disease, the positive likelihood ratio for cirrhosis is 9.5.[9] Although not a common finding, dilated abdominal wall veins have the highest likelihood ratio of all physical examination findings, indicating the presence of cirrhosis (**Fig. 2**).

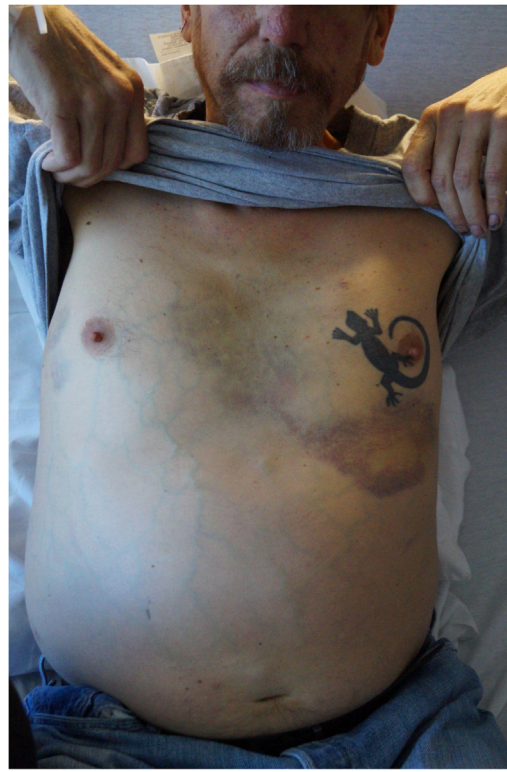

Fig. 2. Dilated abdominal wall veins, bulging flanks, gynecomastia, and ecchymosis in a patient with cirrhosis. (Image courtesy of Paul Aronowitz, MD, Sacramento, CA.)

SPIDER NEVI

Spider nevi are known by a variety of names: arterial spiders, vascular spiders, spider telangiectasias, or spider angiomas (**Fig. 3**). They are named for their appearance, as they have a central erythematous area with multiple "spider legs" made up of arterialized capillaries. They blanch on compression with quick return of blood into the central arteriole following release. Spider nevi are primarily located on the face and neck; less commonly they are found on the shoulders, chest, back, and arms, but they are rarely found below the umbilicus.[17] They are seen in 10% to 15% of healthy children and adults and can be present in other conditions such as pregnancy and rheumatoid arthritis and can be associated with medications such as oral contraceptives.

The presence of multiple spider nevi typically indicates cirrhosis.[18] It is thought that elevated circulating sex hormone activity in the setting of cirrhosis contributes to their development. When diagnosing cirrhosis in a patient with chronic liver disease, the presence of spider nevi has a positive likelihood ratio of 4.2 and negative likelihood ratio of 0.5.[9] In patients with chronic liver disease, spider nevi are more commonly seen in alcoholic patients than nonalcoholic patients. However, the presence of spider nevi correlates with a higher risk of death in patients with cirrhosis from any cause.[19]

PALMAR ERYTHEMA

Palmar erythema refers to symmetric erythema located on the thenar and hypothenar eminences. Similar to spider nevi, palmar erythema is associated with liver disease,

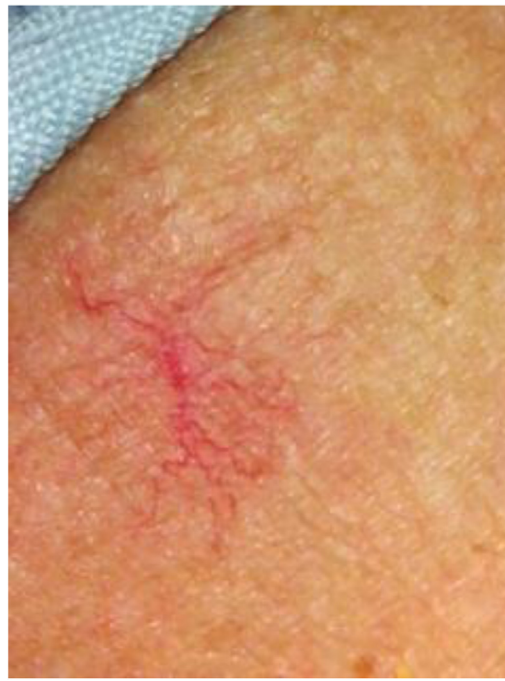

Fig. 3. Spider nevus. (Image courtesy of Paul Aronowitz, MD,Sacramento, CA.)

pregnancy, other less common pathologies, and even can even be hereditary. Although the exact mechanism is unclear, palmar erythema in cirrhotic patients is thought to be related to abnormal serum estradiol to testosterone level and changes in vasculature.[20] If found in patients with underlying liver disease, palmar erythema has a positive likelihood ratio of 3.7, which suggests cirrhosis.[9]

PERIPHERAL EDEMA

Bilateral peripheral pitting edema can result from abnormalities in cardiac, renal, or hepatic function or rarely due to bilateral venous thromboembolic disease. When evaluating edema, the clinical presentation is critical in the determination of the underlying cause. In patients with cirrhosis, low albumin states, especially with serum albumin less than 3.0 g/dL, as well as poor venous return due to pressure on the inferior vena cava from the ascites both contribute to the development of edema. For patients with chronic liver disease, the presence of peripheral edema has a positive likelihood ratio of 3.0, suggesting cirrhosis.[9] As noted when evaluating for ascites, the absence of peripheral edema decreases the probability of ascites with a negative likelihood ratio of 0.2.[12]

ABNORMAL HAIR DISTRIBUTION

Patients with cirrhosis often have reduction in body, axillary, and pubic hair.[21] Hair loss is thought to be related to hormone imbalances involving estrogen and testosterone. Abnormal hair distribution is most common in patients with cirrhosis, and it is not typically found in simple liver disease.[22] If abnormal hair distribution is found in patients

with chronic liver disease, the positive likelihood ratio of having underlying cirrhosis is 8.8.[9]

GYNECOMASTIA

Because of abnormal hormone levels, male patients with cirrhosis can develop gynecomastia. Specifically, gynecomastia is glandular breast tissue that is palpable, 2 to 3 cm in size, and located under the areola. On physical examination, it is important to distinguish between true gynecomastia and fatty tissue deposition. Often, true glandular tissue is tender, whereas adipose tissue is not.[23] If seen in liver disease, gynecomastia has a positive likelihood ratio of 7.0 to diagnose cirrhosis.[9]

BODY HABITUS

Up to 40% of patients with cirrhosis develop muscle wasting. As the underlying pathology progresses, the incidence of wasting increases.[24] Multiple factors contribute to the development of muscle wasting including poor nutrition, altered protein metabolism, the liver's inability to successfully regulate protein production, and modified absorption of nutrients in the bowels.[1] As a result, cirrhotics can live in a catabolic state and are often cachectic on examination with significant, diffuse muscular atrophy.

TESTICULAR ATROPHY

Testicular atrophy may be present in patients with a variety of underlying conditions, including cirrhosis, low testosterone states, or postsurgical complications after inguinal surgery repair. If other physical examination findings suggest cirrhosis, this diagnosis should be considered. Approximately 40% to 50% of men with cirrhosis will develop testicular atrophy and gynecomastia.[25] These changes occur in the setting of hormone imbalances related to the underlying cirrhosis.

TERRY NAILS

Terry nails are found in patients with cirrhosis, congestive heart failure, diabetes, or increased age.[26] Bilaterally, the nails seem white at the base with extension toward the distal nail. The white discoloration can conceal the underlying lunula and progress to cover the entire nail bed except the distal 1 to 2 mm. These findings are most prominently found in the thumb and index finger.[27]

FETOR HEPATICUS

Dimethyl sulfide in the breath causes a characteristic odor in cirrhotic patients known as fetor hepaticus.[28] The smell is distinct and described as an odor similar to a mixture of garlic and rotten eggs. Although not a common finding, its presence is due to shunting in the setting of cirrhosis rather than actual liver failure or encephalopathy.[9]

SUMMARY

The physical examination can be helpful in identifying patients who have underlying cirrhosis, especially if historical features such as alcohol or drug use, known diagnosis of viral hepatitis, or obesity are present. Many patients with cirrhosis have compensated disease, which can be present chronically without the need for hospitalization. Decompensated cirrhosis, including the presence of ascites, acute gastrointestinal bleeding often from esophageal varices, and hepatic encephalopathy, often drives

patients to seek emergency care and frequently requires hospitalization. Early identification of physical findings that suggest cirrhosis can guide the clinician to order testing aimed at determining the underlying cause of cirrhosis, provide lifestyle counseling to avoid progression of disease, and suggest appropriate treatment and screening recommendations.

CLINICS CARE POINTS

- When evaluating patients with chronic liver disease for the presence of cirrhosis, the liver examination with the highest likelihood ratio to indicate cirrhosis is a firm liver edge on palpation, which has a positive likelihood ratio of 3.3.[9]
- Jaundice in the setting of chronic liver disease has a positive likelihood ratio of 3.8, supporting the diagnosis of cirrhosis whereas the negative likelihood is 0.8.[9]
- When assessing a patient for the presence of ascites, the fluid wave has the highest positive likelihood ratio of 5.0. Shifting dullness follows this with a positive likelihood ratio of 2.3.
- If encephalopathy is present in patients with chronic liver disease, the likelihood ratio for underlying cirrhosis is 8.8.[9]
- Although not a common finding, dilated abdominal veins have the highest likelihood ratio of all physical examination findings of cirrhosis with a positive LR of 9.5.[9]
- When diagnosing cirrhosis in a patient with chronic liver disease, the presence of spider nevi has a positive likelihood ratio of 4.2 and negative likelihood ratio of 0.5.[9]
- If abnormal hair distribution is found in patients with chronic liver disease, the positive likelihood ratio of having underlying cirrhosis is 8.8.[9]

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