Chapter 4

Cirrhosis

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Cirrhosis

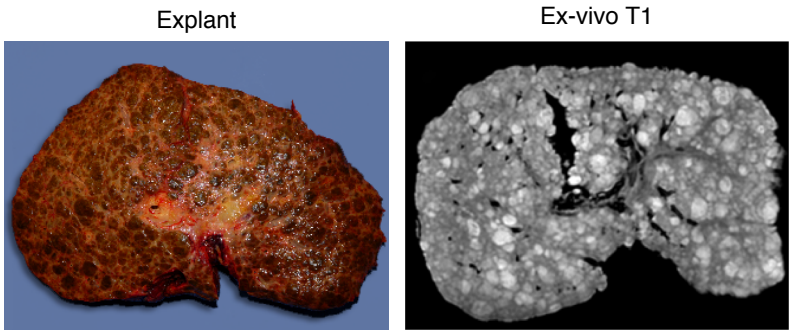
Introduction

This chapter reviews in question and answer format the imaging manifestations of cirrhosis. Understanding these manifestations is essential to the proper application of LI-RADS for the following reasons:

- Cirrhosis is the primary risk factor for developing hepatocellular carcinoma (HCC).
- In patients with cirrhosis, multiphase CT and MRI performed and interpreted according to LI-RADS specifications can establish the diagnosis of HCC definitively, obviating the need for invasive biopsy and histologic confirmation.
- Cirrhosis-associated abnormalities in and outside the liver may reduce diagnostic accuracy:
  - Hepatic pseudolesions, parenchymal heterogeneity, and background nodularity may reduce sensitivity (see *page 4-5*).
  - Altered imaging appearance of both benign and malignant lesions may confound interpretation.
  - Extrahepatic abnormalities may reduce image quality (see *page 4-5*).

What is cirrhosis?

- Cirrhosis is an advanced stage of chronic liver disease resulting from repetitive liver injury and cumulative liver damage.
- Cirrhosis is characterized by the complete replacement of normal parenchyma by innumerable regenerative nodules surrounded by fibrotic bands (“scars”).



Innumerable parenchymal regenerative nodules with intervening fibrosis = cirrhosis

- Cirrhosis may be accompanied by profound alterations in the hepatic microcirculation with formation of abnormal microscopic connections between hepatic arterioles and portal venules, so-called arterioportal shunts.
- Additionally, there is variable loss of hepatocellular function, depending on the severity of parenchymal damage.

Background

What causes cirrhosis?

- The causes of cirrhosis and their prevalence vary geographically.
- In the United States, the most common etiologies of cirrhosis are nonalcoholic steatohepatitis (NASH), chronic hepatitis C virus (HCV), and excess alcohol consumption. Other relatively common etiologies include chronic hepatitis B virus (HBV), hereditary hemochromatosis (HH), primary biliary cholangitis (PBC), and autoimmune hepatitis (AIH).

Why is cirrhosis clinically important?

- Cirrhosis has a wide clinical and pathophysiologic spectrum, ranging from normal function to fulminant hepatic failure.
- Cirrhosis can cause morbidity and mortality due to complications such as hepatic dysfunction, liver failure, and portal hypertension.
- Cirrhosis is also a major risk factor for primary liver cancer, especially HCC:
  - About 80% of HCC cases develop in patients with cirrhosis.
  - Patients with cirrhosis have a 2-8% annual risk of developing HCC.
  - HCC incidence depends on the etiology of cirrhosis and the presence of additional risk factors.
- Compared to the general population, patients with cirrhosis and other chronic liver diseases are also at increased risk for developing:
  - Intrahepatic cholangiocarcinoma (iCCA)
  - Combined hepatocellular-cholangiocarcinoma (cHCC-CCA)

Most common malignant neoplasms associated with cirrhosis and their definitions

Malignancy	Definition
Hepatocellular carcinoma (**HCC**)	Malignant neoplasm with hepatocytic differentiation (cytology and architecture)
Intrahepatic cholangiocarcinoma (**iCCA**)	Malignant neoplasm with cholangiocytic differentiation (cytology and architecture)
Combined hepatocellular and cholangiocarcinoma (**cHCC-CCA**)	Malignant neoplasm with varying degrees of hepatocytic and cholangiocytic differentiation, either admixed or as separate areas within the same tumor (cytology and architecture)

For more information on these neoplasms, *see Chapter 5*

Background

How does cirrhosis affect options for and outcomes of treatment of HCC and other primary liver carcinomas such as iCCA and cHCC-CCA?

- Cirrhosis limits options for and outcomes of treatment of HCC.
- Underlying liver dysfunction reduces hepatic reserve, which precludes surgical resection in most patients and increases morbidity after locoregional treatment.
- Even after successful surgical or locoregional treatment for HCC, the background liver remains a source for future HCCs.

Is there a curative option for HCC?

- The only way to cure HCC and reduce risk of recurrence is transplantation
- By replacing the cirrhotic liver with a healthy organ, liver transplantation restores function and reduces the risk of future cancer.
- Due to donor organ scarcity, however, only a minority of transplant candidates receive a transplant.
- As biopsy confirmation of imaging-diagnosed HCCs is not required, transplantation for HCC cure requires high imaging specificity to allocate donor organs appropriately.

What is the annual incidence of HCC associated with the commonest etiologies of cirrhosis?

Etiology	Annual HCC incidence
HCV	2-8%
HBV	2.5%
Alcohol	1%
Nonalcoholic steatohepatitis	2%
Hereditary hemochromatosis	3-4%
Primary biliary cholangitis	2%
Auto-immune hepatitis	?

- In the above conditions, the risk of HCC is sufficiently high that HCC surveillance is warranted and LI-RADS is applicable for noninvasive diagnosis of HCC (see *Chapter 2, page 5*).
- Risk factors are additive, and patients with multiple risk factors are at higher risk.

Background

Besides cirrhosis, what are other risk factors for HCC development?

- Other risk factors include
  - Precirrhotic chronic HBV – even in the absence of cirrhosis, the risk of HCC in adult chronic HBV carriers can be sufficiently high to warrant HCC surveillance and to justify the use of LI-RADS for noninvasive diagnosis of HCC.
  - Precirrhotic chronic HCV
  - Precirrhotic NASH
  - Excess alcohol consumption, obesity, diabetes, old age, male sex, smoking, family history of HCC

In the absence of cirrhosis, the risk of HCC is too low to warrant surveillance for HCC (surveillance is not considered cost effectives) or to justify the use of LI-RADS for noninvasive diagnosis of HCC

- *See Chapter 2* for more information

Is cirrhosis reversible?

- Early cirrhosis is potentially reversible.
- Advanced end-stage cirrhosis is irreversible: while some of the scars may regress if the inciting cause is removed, the liver will not return to normal structure or function.

Does cirrhosis reversal reduce HCC risk?

- Reversal of cirrhosis is thought to reduce HCC risk but the magnitude of the reduction is not well understood.
- In particular, it is not known when the risk falls low enough that surveillance is no longer indicated or that application of diagnostic CT/MRI LI-RADS is no longer applicable.
- This is an area for future research; little is currently known about the impact of novel anti-viral and anti-fibrotic therapies on HCC risk.

Does clearance of HBV and HCV reduce HCC risk?

- Effective treatments for HBV and HCV are now available. These treatments can result in a sustained viral response.
- Similar to cirrhosis reversal, clearance of HBV and HCV is thought to reduce HCC risk but the magnitude of the reduction is not well understood.
- This is an area for future research; little is currently known about the impact of novel anti-viral and anti-fibrotic therapies on HCC risk

Background

Why is cirrhosis relevant to HCC imaging?

- Cirrhosis is relevant to HCC imaging for two major reasons:
  - Cirrhosis portends a high enough pre-test probability of HCC to allow non-invasive imaging diagnosis of HCC.
  - Cirrhosis-associated abnormalities may reduce diagnostic accuracy for HCC.
- These factors are discussed below:

Cirrhosis portends a high enough pre-test probability of HCC to allow non-invasive imaging diagnosis of HCC

For most etiologies of cirrhosis (*see page 4-2*), the pre-test probability of HCC and of non-malignant lesions resembling HCC is sufficiently high and low, respectively, that lesions meeting stringent HCC imaging criteria can be confidently assumed to be HCC.

This enables diagnosis of HCC based on imaging alone. Biopsy confirmation of imaging-diagnosed HCCs is not required routinely, although biopsy may still be desired in some situations (e.g., for molecular characterization, or if needed for a clinical trial).

Imaging-based diagnosis of HCC may be difficult in the patient with cirrhosis, however (see below).

Cirrhosis-associated abnormalities may reduce diagnostic accuracy for HCC

Vascular pseudolesions and non-tumoral parenchymal lesions may obscure small masses (reducing sensitivity) or may be mistaken for HCC (reducing specificity). These include:

- Arterioportal shunt (*Chapter 15, page 25*), confluent hepatic fibrosis (*Chapter 15, page 18*), focal scar (*Chapter 15, page 23*), hepatic hypertrophic pseudomass (*Chapter 15, page 21*), hepatic parenchymal fat deposition (*Chapter 15, page 14*).

The cirrhotic liver also contains a spectrum of nodules with wide-ranging imaging manifestations and biological behaviors. These further complicate HCC imaging (see *Chapter 5, page 2*).

Liver dysfunction may lead to inadequate hepatobiliary contrast agent uptake.

Third spacing may dilute intravascular contrast material, reduce the magnitude of vascular, parenchymal, and tumor enhancement, and compromise the quality of enhanced images.

Hemodynamic vascular alterations may delay the arrival of contrast material to the liver and to the tumor, potentially causing arterial phase mistiming.

Ascites may cause severe artifacts at MRI, obscuring true lesions in or outside the liver.

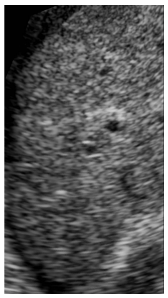
Encephalopathy and other co-morbidities may decrease patient compliance.

Imaging Manifestations of Cirrhosis

What are the Imaging manifestations of cirrhosis?

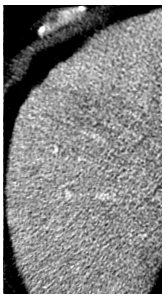
- The cirrhotic liver is carved into innumerable nodules by fibrous scars. Since the nodules and scars may be imperceptible, however, the cirrhotic liver may appear normal at imaging.
- ⚠ ***Thus, a normal-appearing liver at US, CEUS, MRI, or CT does not exclude cirrhosis.***

US



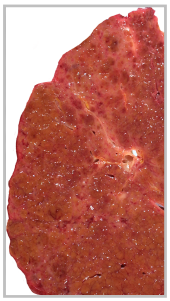
Coarsened echotexture without discrete parenchymal nodules

CT



Minimal surface nodularity without discrete parenchymal nodules

Explant

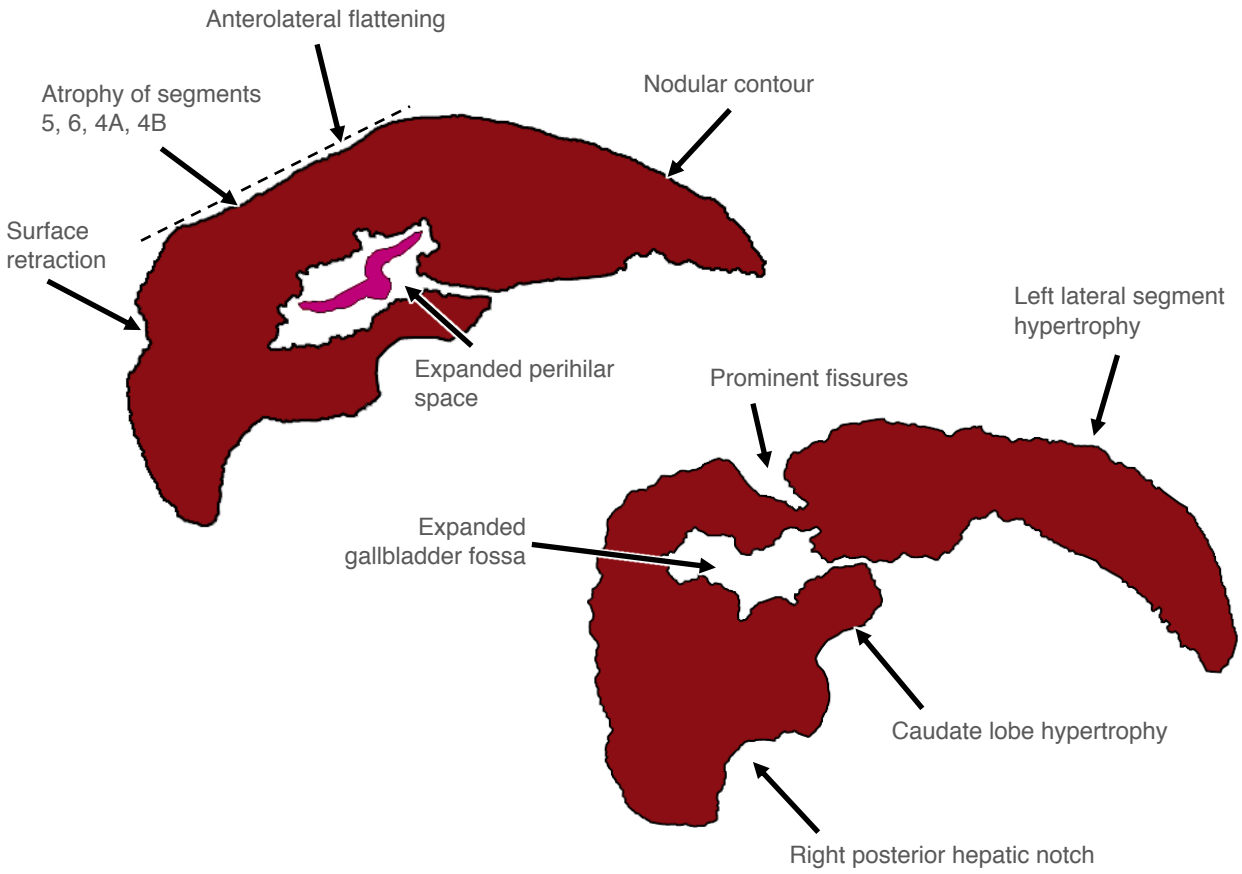


Numerous nodules with intervening fibrosis = cirrhosis

- Certain morphological, parenchymal, vascular, biliary, and extrahepatic alterations of cirrhosis may be visible at imaging, however, especially if the cirrhosis is advanced or long standing.
- These alterations and their imaging manifestations are listed in the next several tables.
- By being familiar with these imaging findings, radiologists may be alerted to the possibility of cirrhosis even if the history is omitted or unknown.
- 💡If the presence of cirrhosis can then be confirmed – for example by reviewing the electronic medical record or by communicating with the referrer – LI-RADS can be applied.
- 💡If the presence of cirrhosis cannot be confirmed but the imaging findings are compelling, LI-RADS can be applied conditionally: e.g., “If the patient has cirrhosis, the observation meets criteria for LR-5, definitely HCC”.

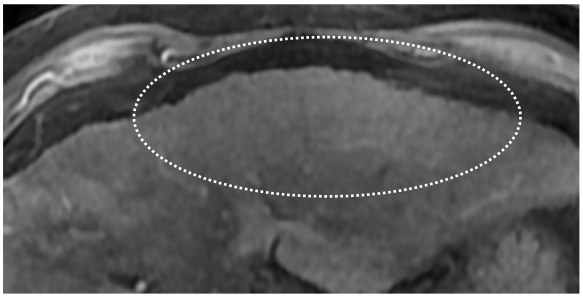
Imaging Manifestations of Cirrhosis

Morphological alterations of cirrhosis that may be evident at imaging

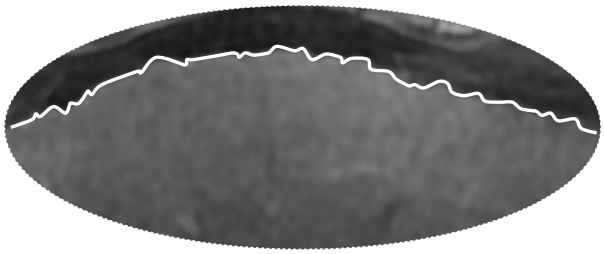


Morphological alteration	Imaging manifestation

Presence of regenerative nodules immediately under liver capsule	• Surface nodularity
	  • High specificity for cirrhosis in right clinical setting.
	  • ⚠ Specificity is imperfect, however, as some non-cirrhotic conditions may manifest surface nodularity (see page 4-18).
	  • Provides low sensitivity for early cirrhosis (liver may be smooth)



Surface nodularity

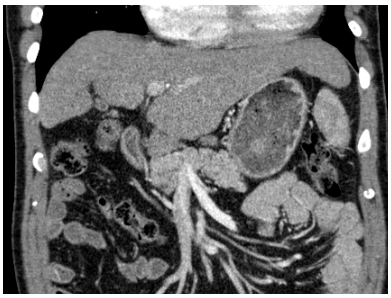


Imaging Manifestations of Cirrhosis

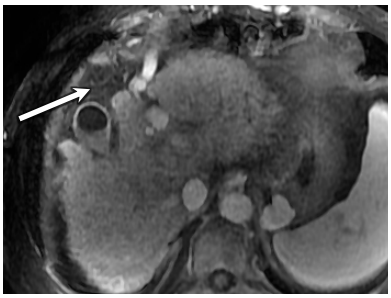
Morphological alterations of cirrhosis that may be evident at imaging (Cont'd)

Morphological alteration	Imaging manifestation

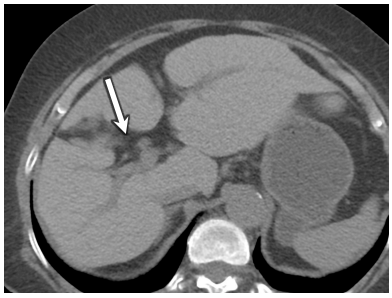
Global atrophy	• Small liver volume
	• Generalized hepatic contraction with expansion of following spaces
	  • Space between liver and anterior abdominal wall
	  • Perihilar, gallbladder fossa and ligamentum teres spaces



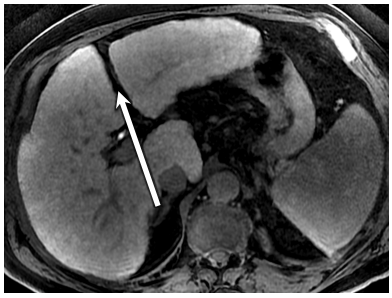
Small liver volume



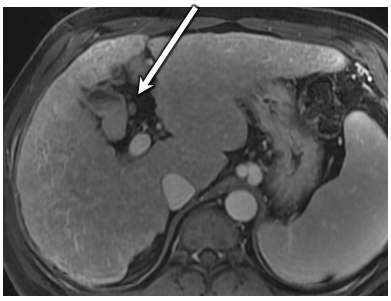
Expansion of the space between liver and anterior abdominal wall



Expansion of perihilar space



Expansion of ligamentum teres space

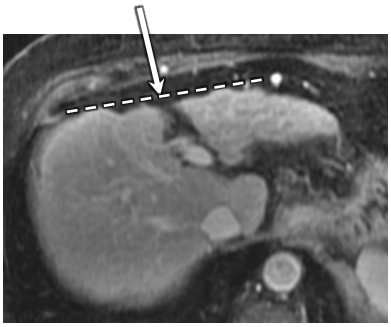


Expansion of gallbladder fossa

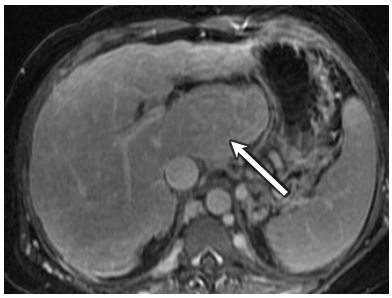
Imaging Manifestations of Cirrhosis

Morphological alterations of cirrhosis that may be evident at imaging (Cont'd)

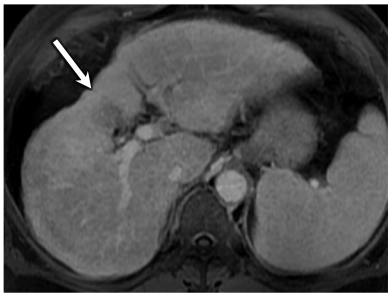
Morphological alteration	Imaging manifestation
Segmental volume redistribution	• Relative or absolute hypertrophy of caudate (S1) and/or lateral left section (S2 and S3) • Atrophy of anterior right section (S5, S6) and/or medial left section (S4A and S4B) • Increased caudate-right lobe ratio • Anterolateral flattening
Regional or focal parenchymal contraction	• Notching of posterior right lobe, medially • Liver surface retraction associated with areas of confluent fibrosis



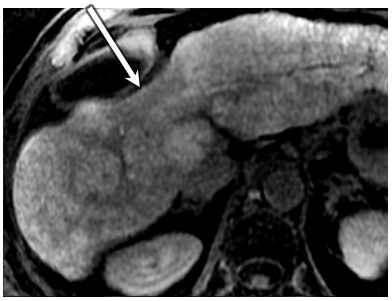
Anterolateral flattening



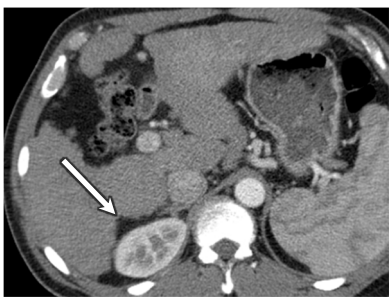
Hypertrophy of the caudate lobe



Atrophy of medial left (S4A-4B)



Liver surface retraction



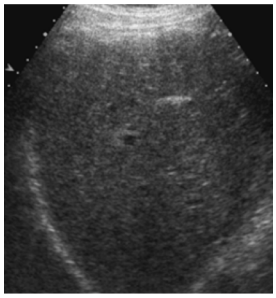
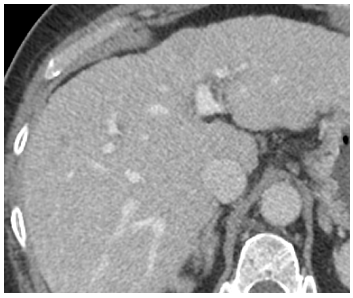
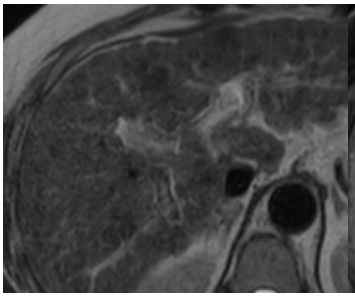
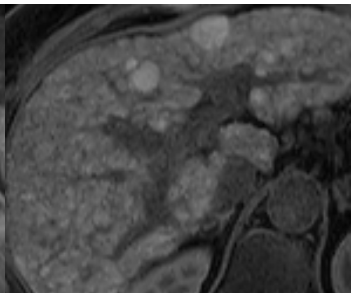
Notching of the posterior right lobe

Imaging Manifestations of Cirrhosis

Parenchymal alterations of cirrhosis that may be evident at imaging

Parenchymal alteration	Imaging manifestation
Parenchymal nodules	• Parenchymal nodules may be visible. If visible, these vary widely in size and other imaging features. See *Chapter 5, page 2*

US | PVP CT | T2 | Pre

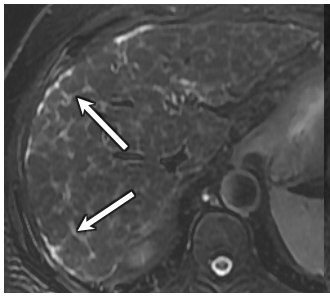
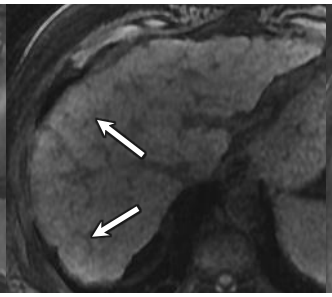
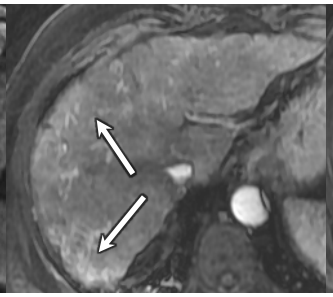
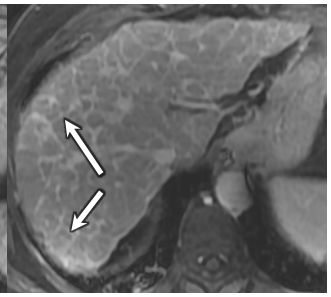





Discrete parenchymal nodules are not discerned

Numerous parenchymal nodules of variable size and variable signal on both T1w and T2w

Fibrotic scars surrounding parenchymal nodules (scars typically have high water content and are devoid of hepatocytes)	• May be visible at CT or MRI as a diffuse lacework of thin bands. • Tend to be mildly hypoattenuating on unenhanced CT, hypointense on T1w images, hyperintense on T2w and low-b-value DW images • Enhance progressively on dynamic vascular phases to become hyperattenuating or hyperintense in the PVP and DP • Tend to be hypointense on HBP T1w images • Usually imperceptible on ultrasound although they may contribute to generalized parenchymal heterogeneity

T2 | Pre | AP | DP

High signal

Low signal

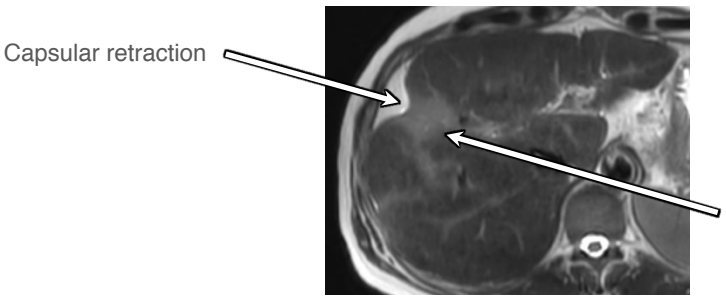
Little or no enhancement on AP

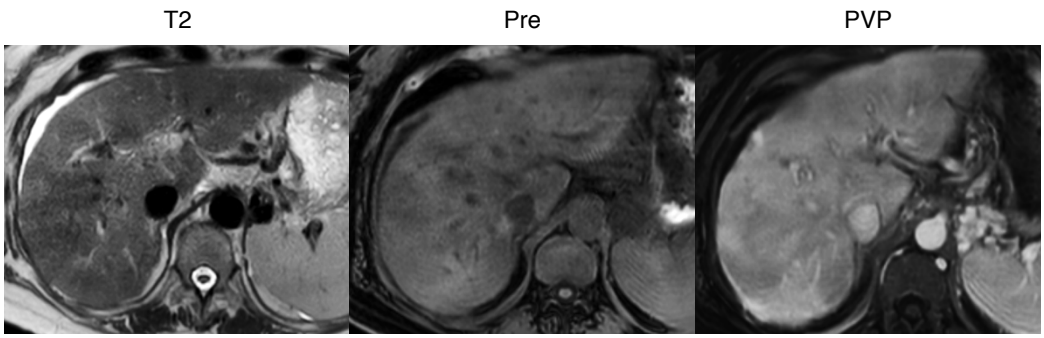
Enhancement on DP

Imaging Manifestations of Cirrhosis

Parenchymal alterations of cirrhosis that may be evident at imaging (Cont'd)

Parenchymal alteration	Imaging manifestation
Confluent hepatic fibrosis (broad, mass-like areas of scar tissue) *Chapter 15, page 18*	• Characteristically pyramidal in shape with concave borders • Radiate from hilum to liver periphery • Retract liver surface • Similar intensity and enhancement characteristics as fibrotic scars • May resemble iCCA, a typically fibrotic tumor that similarly may be retractile and show progressive dynamic-phase enhancement • Key difference: confluent fibrosis lacks densely cellular and vascularized rim, and so, does not have targetoid appearance typical of iCCA. See *Chapter 16, page 205* for targetoid appearance.
Nonspecific parenchymal heterogeneity	• If the above parenchymal alterations are beneath the size threshold of imaging, the parenchyma may appear mottled or coarse without distinct internal nodularity or scarring.





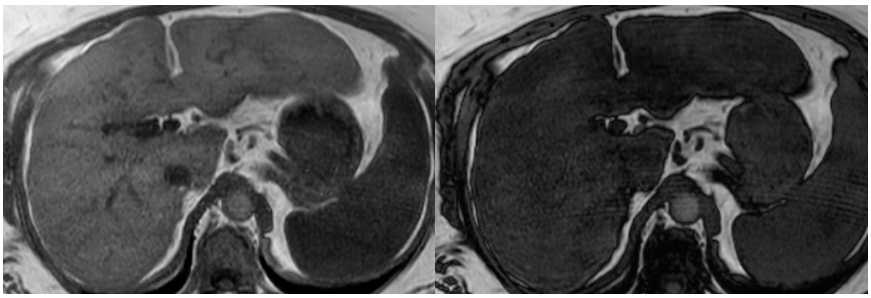
Heterogeneous and mottled parenchyma on various sequences

Imaging Manifestations of Cirrhosis

Parenchymal alterations of cirrhosis that may be evident at imaging (Cont'd)

Parenchymal alteration	Imaging manifestation
Fat	• Diffuse, regional, or focal hepatic fat accumulation (steatosis). • Frequently occurs in NASH, alcoholic liver disease, hepatitis due to certain genotypes of HCV • Fat regresses as cirrhosis progresses and hepatocellular function worsens. The heavily scarred, end-stage liver is devoid of fat.

IP (TE = 4.6 ms) OP (TE = 2.3 ms)

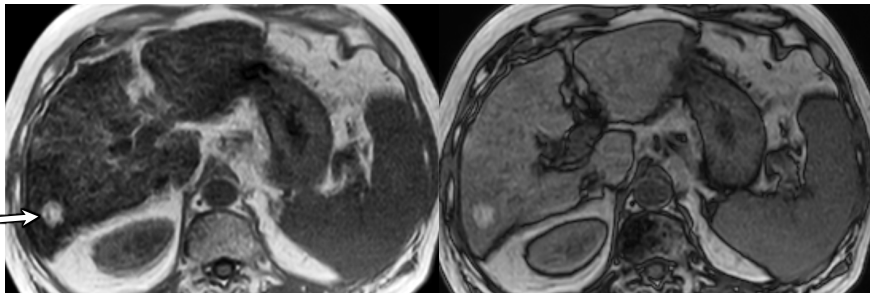


Diffuse loss of signal in the liver parenchyma on the opposed phase compared with in phase sequence confirms steatosis

Iron	• Diffuse, regional, or focal hepatic iron overload (siderosis).
	  • Cirrhosis due to hereditary hemochromatosis is almost always associated with iron overload.
	  • Cirrhosis due to other chronic liver disease (e.g., HBV, HCV, alcohol-induced liver disease, NASH) may be associated with iron overload.

IP (TE = 4.6 ms) OP (TE = 2.3 ms)

Note observation with iron sparing (ancillary feature favoring malignancy (see *Chapter 16, page 289*)



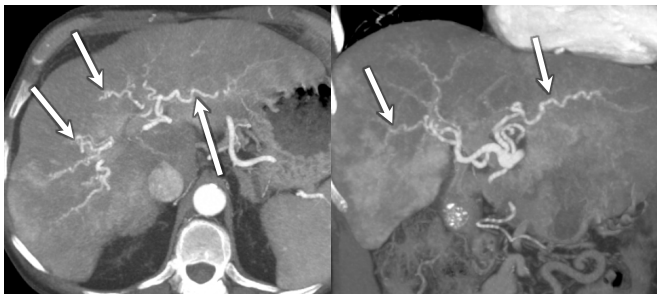
Diffuse loss of signal in the liver parenchyma on the longer echo GRE sequence compared with shorter echo sequence confirms iron deposition

Imaging Manifestations of Cirrhosis

Vascular alterations of cirrhosis that may be evident at imaging

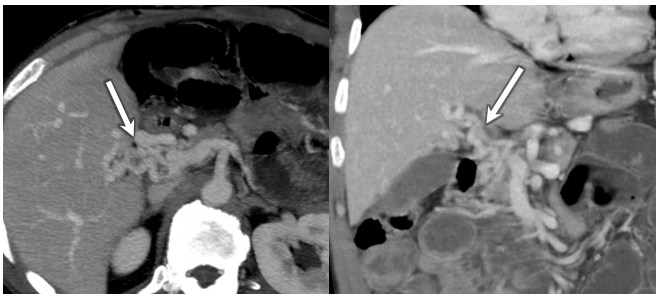
- Hepatic artery enlargement, ± tortuosity (corkscrew appearance)
- Portal vein and/or portal vein branch
  - dilation (≥ 15 mm in diameter for main portal vein)
  - caliber reduction with long-standing reduction in portal flow
  - chronic thrombosis
  - chronic sclerosis
- Distortion of intrahepatic veins including narrowing of intrahepatic cava and hepatic veins
- Formation of intrahepatic and extrahepatic portal-systemic collaterals (see below)
- Development of microcirculatory arterioportal shunts (see *Chapter 15, page 25*)
- Cavernous transformation with occlusion or near occlusion of portal vein or its major branches

Axial AP | Coronal MPR AP



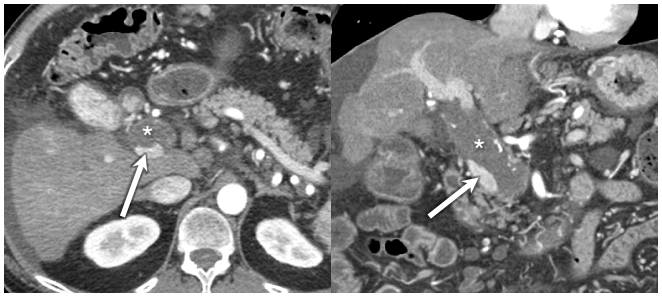
Tortuous intrahepatic arteries (corkscrew appearance)

Axial AP | Coronal MPR AP



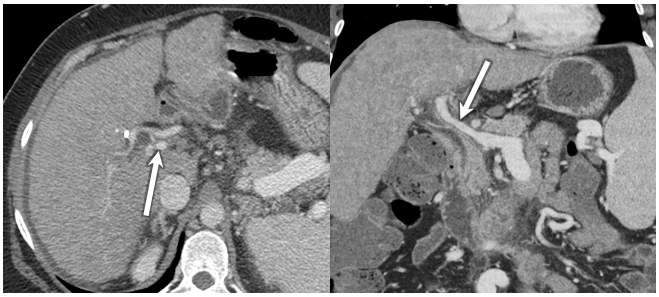
Multiple tortuous collaterals in the expected location of the main portal vein (chronic PV thrombosis with cavernous transformation)

Axial AP | Coronal MPR AP



Dilated main portal vein (3 cm in diameter) with a thrombus (*) and narrowed lumen (arrow); calcifications in the periphery of thrombus indicate chronicity

Axial AP | Coronal MPR AP



Attenuated main portal vein (0.6 cm in diameter)

Imaging Manifestations of Cirrhosis

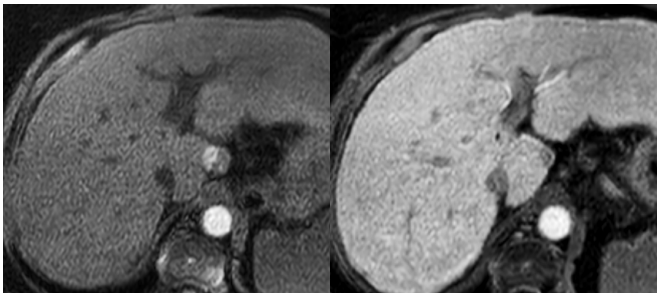
Functional alterations of cirrhosis that may be evident at imaging with hepatobiliary agents

Altered expression levels of hepatocyte transporters

- Reduced expression of hepatocyte bilirubin (organic anion transporting polypeptide, OATP) transporters, sometimes with preserved or even enhanced expression of hepatocyte nonspecific (multidrug resistant associated protein, MRP) exporters.
- Depending on the balance of hepatocellular uptake and excretion, as well as other factors, there may be diminished enhancement of the liver parenchyma during the hepatobiliary phase after administration of a hepatobiliary agent with preserved enhancement of the bile duct lumen.
- ⚠Thus, enhancement of the bile duct lumen does *not* indicate adequate hepatocellular uptake for diagnosis of HCC.
- See *Chapter 13.*

Adequate HBP

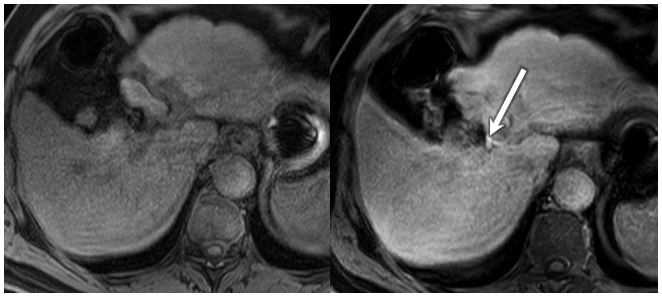
Pre | 20 min HBP



Enhancement of the parenchyma greater than the intrahepatic vasculature

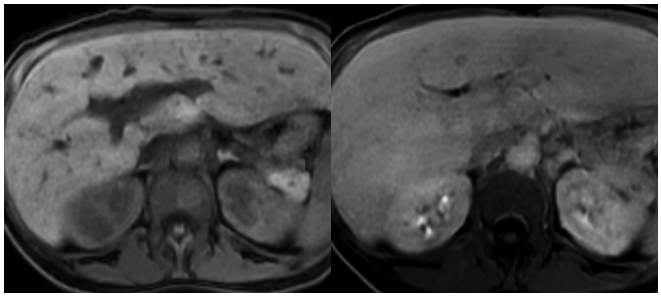
Suboptimal HBP

Pre | 20 min HBP



Parenchyma enhances similar to the intrahepatic vessels; note the preserved gadoxetate excretion in the bile ducts (arrow)

Pre | 20 min HBP



Parenchyma enhances similar to the intrahepatic vessels; no gadoxetate excretion in the bile ducts

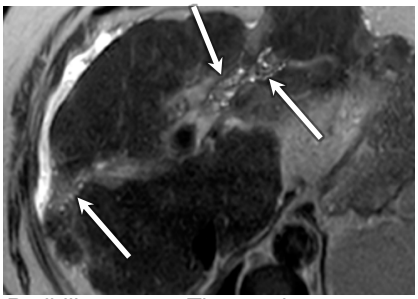
Imaging Manifestations of Cirrhosis

Biliary alterations of cirrhosis that may be evident at imaging

Peribiliary cysts

- Representing cystic dilatation of obstructed periductal glands, these tubular structures parallel the large intra and extrahepatic bile ducts and are located on both sides of the intrahepatic portal vein branches.
- These rare lesions are markedly hyperintense on T2w images and have imperceptible, non-enhancing walls.
- No communication with the biliary tree is evident after administration of hepatobiliary agents.

T2



Peribiliary cysts: Tiny cystic structures along the portal venous branches

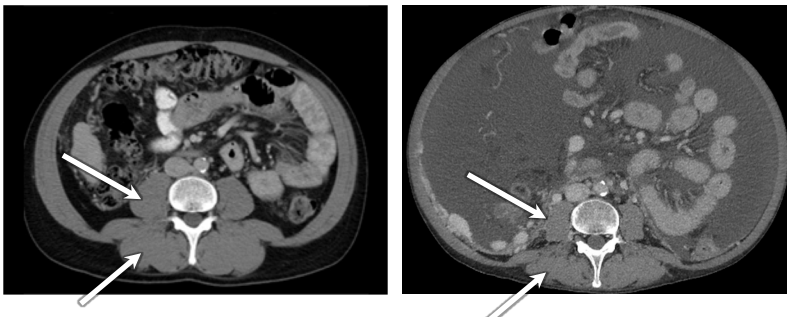
Musculoskeletal manifestations that may be evident at imaging

Sarcopenia

- Progressive and profound atrophy of abdominal wall, psoas, and paraspinal muscles may be evident

Initial CT

CT 4 years later



Normal psoas and paraspinal muscles

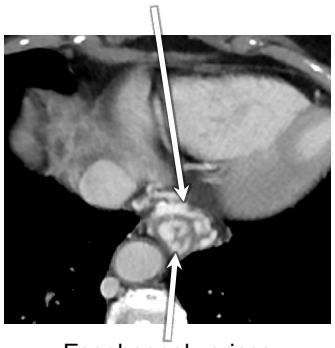
Atrophy of psoas and paraspinal muscles

Imaging Manifestations of Cirrhosis

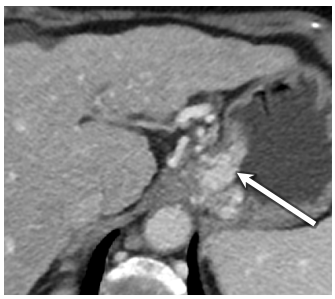
Manifestations of portal hypertension that may be evident at imaging

Portal-systemic collaterals	• esophageal • paraesophageal • left gastric • retrogastric • gastrorenal • perisplenic • splenorenal • paraumbilical • caput Medusae • paravertebral (retroperitoneal) • hemorrhoidal

Paraesophageal varices

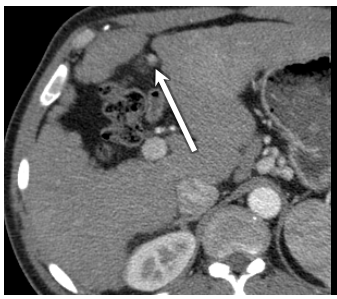


Esophageal varices

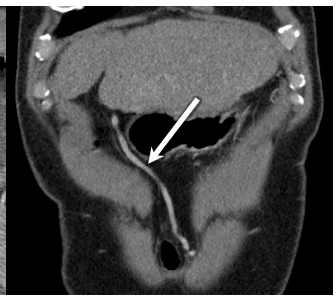


Gastric varices

Axial

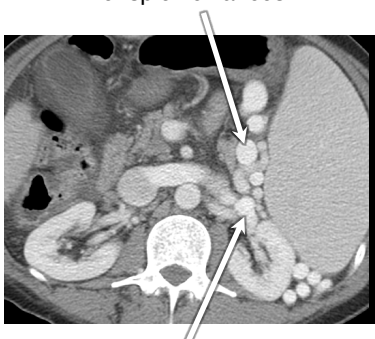


Coronal



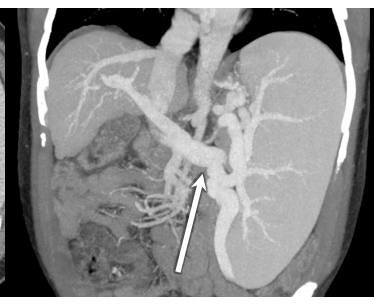
Recanalized paraumbilical vein: within the ligamentum teres space, extending toward the umbilicus

Perisplenic varices

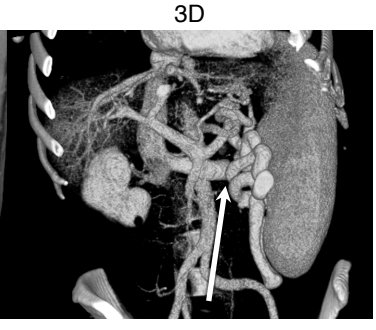


Splenorenal shunt

MIP



3D

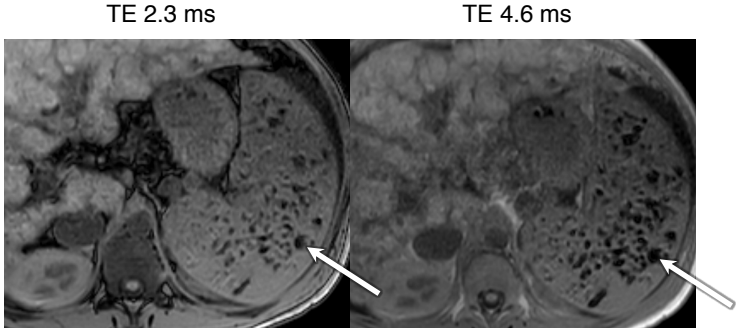


Splenorenal shunt

Imaging Manifestations of Cirrhosis

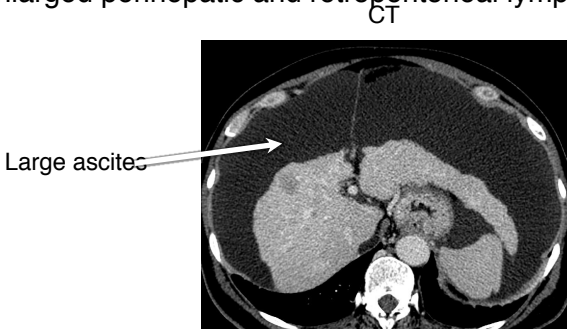
Manifestations of portal hypertension that may be evident at imaging (Cont'd)

Spleen	• Splenomegaly • Gamna-Gandy bodies: small deposits of iron and calcium within fibrous and elastic fibers in the spleen from microhemorrhages due to portal hypertension.

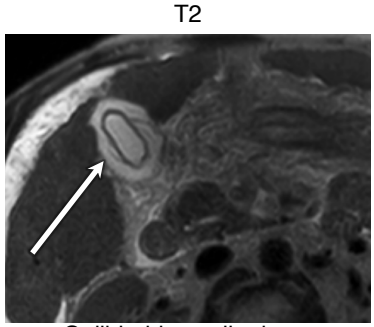


Gamna-Gandy bodies: numerous foci of signal void, more pronounced on the longer echo GRE sequence

Fluid retention	• ascites • mesenteric, omental and retroperitoneal edema • enlarged perihepatic and retroperitoneal lymphatics



Submucosal edema	• wall thickening of	• gallbladder • stomach (portal gastropathy) • jejunum • right colon (portal colopathy)



Gallbladder wall edema

Frequently Asked Questions

Are there any etiology-specific imaging manifestations?

Certain imaging features are characteristic of particular etiologies of cirrhosis although they are not specific enough to render a definitive diagnosis

Size	• Alcoholic liver disease, non-alcoholic fatty liver disease, primary biliary cirrhosis: cirrhotic liver may be diffusely enlarged. It does not become globally atrophic until cirrhosis is advanced • Viral hepatitis: cirrhotic liver is usually small, even in early cirrhosis
Segmental volume redistribution	• Alcoholic liver disease: caudate enlargement and right posterior hepatic notch • Primary sclerosing cholangitis (PSC): massive enlargement of central portions of the liver with severe atrophy of the liver periphery
Confluent hepatic fibrosis	• Alcoholic liver disease, PSC
Other	• PSC: biliary stricturing and fibrosis, patchy peribiliary enhancement due to active cholangitis • Congenital hepatic fibrosis: biliary sacculations (as well as renal tubular ectasia) • Primary biliary cirrhosis: periportal haloes • Wilson disease: honeycomb pattern of ≥ 10 mm regenerative nodules • Alcoholic liver disease, non-alcoholic fatty liver disease, certain genotypes of hepatitis C viral infection: steatosis (in early cirrhosis)

What conditions other than cirrhosis may manifest with liver surface nodularity?

Although liver surface nodularity is the most specific imaging feature of cirrhosis, conditions other than cirrhosis may be associated with liver surface nodularity.

Examples of conditions other than cirrhosis that may be associated with liver surface nodularity	• “Pseudo-cirrhosis” in patients with treated metastases • Regeneration after massive hepatic failure • Miliary metastases • Sarcoidosis • Diffuse nodular regenerative hyperplasia

Frequently Asked Questions

Can cirrhosis be diagnosed on conventional imaging?

- When present in the appropriate clinical context, liver surface nodularity, segmental volume redistribution, and other morphological and parenchymal alterations described earlier suggest the possibility of cirrhosis.
- However, no feature is sufficiently specific to permit a reliable diagnosis of cirrhosis by itself.
- Thus,

  the diagnosis of cirrhosis should not be rendered based on imaging in a clinical vacuum

  while radiologists may suggest the possibility of cirrhosis if there is definite liver surface nodularity, non-invasive diagnosis requires that the clinical and laboratory features are consistent with cirrhosis.

Are there advanced quantitative imaging methods to diagnose cirrhosis?

- Advanced quantitative imaging methods to diagnose cirrhosis have been developed. The leading method for this purpose is **MR elastography (MRE),** discussed briefly below**.** Other methods are described in the referenced articles at the end of the chapter.
- MRE estimates the stiffness of the liver indirectly by analyzing the propagation of shear waves through the liver. The stiffness is reported in kiloPascals or kPa. The central concept is that as fibrosis (scarring) develops, the liver becomes progressively stiffer, because the fibrotic tissue imparts rigidity. A stiffness value ≥ 3.6 kPa indicates with with high sensitivity and specificity the presence of advanced fibrosis (either severe fibrosis or cirrhosis). MRE can be done on routine clinical MR scanners but requires the acquisition of specialized hardware to generate the shear waves and software to visualize and analyze the shear waves.

Are there any blood tests that can diagnose cirrhosis?

- Many blood tests or combinations of blood tests can be used to diagnose cirrhosis.
- One of the simplest is the AST to platelet ratio index (APRI). The key concept is that the combination of a high AST (large numerator) and low platelet count (small denominator) indicates advanced fibrosis.
- Although APRI is not accurate as advanced imaging methods such as MRE for diagnosis of fibrosis it is based on common, routine blood tests.
- An elevated APRI can increase the radiologist's diagnostic confidence about the presence of cirrhosis if imaging features of cirrhosis are equivocal.

Frequently Asked Questions

What is nodular regenerative hyperplasia (NRH), what causes it, and how is it diagnosed?

Definition

In NRH, small (usually 1 mm) regenerative nodules are diffusely encountered throughout the hepatic parenchyma. Fibrosis is minimal or absent (the presence of fibrous septa between the nodules excludes the diagnosis of NRH).

Causes

NRH develops as response to anomalous portal hepatic blood flow that can occur in a large number of conditions including autoimmune, inflammatory and neoplastic diseases and exposure to immusuppressant and chemotherapeutic drugs.

NRH and non-cirrhotic intrahepatic portal hypertension (NCIPH)

In NCIPH the blood flow obstruction occurs in the intrahepatic portal venous branches (the main portal vein is patent and there is no cirrhosis). NRH is one of the histological entities that can be seen in NCIPH – other entities include sinusoidal obstruction syndrome, perisinusoidal fibrosis, hepato-portal sclerosis, incomplete fibrotic septa.

NRH and LI-RADS

NRH is relevant to LI-RADS because the associated morphologic changes may mimic cirrhosis. The available published data on the imaging appearance of NRH is scant and the diagnostic accuracy limited.

Summary

Cirrhosis is the primary risk factor for developing HCC.

In patients with cirrhosis, multiphase CT and MRI performed and interpreted according to LI-RADS can establish the diagnosis of HCC definitively, obviating the need for invasive biopsy and histologic confirmation. The premise is that the pre-test probability of HCC and of non-malignant lesions resembling HCC is sufficiently high and low, respectively, that lesions meeting stringent HCC imaging criteria can be confidently assumed to be HCC.

Although cirrhosis allows the application of noninvasive imaging to diagnose HCC, cirrhosis-associated abnormalities in and outside the liver may reduce diagnostic accuracy.

Cirrhosis is an advanced stage of chronic liver disease resulting from repetitive liver injury and cumulative liver damage. It is characterized by the complete replacement of normal parenchyma by regenerative nodules surrounded by fibrotic bands (“scars”), alterations in the hepatic microcirculation, and variable loss of hepatocellular function.

In the United States, the most common etiologies of cirrhosis are NASH, chronic HCV, and excess alcohol consumption. Other relatively common etiologies include chronic HBV, hereditary hemochromatosis (HH), primary biliary cholangitis (PBC), and autoimmune hepatitis (AIH)

Besides cirrhosis, there are many other risk factors for HCC development, including HBV carrier state without cirrhosis, precirrhotic HCV, precirrhotic NASH, excess alcohol consumption, obesity, diabetes, old age, male sex, smoking, family history of HCC. Other than HBV carrier state, none has been shown to elevate the risk sufficiently to apply LI-RADS.

The cirrhotic liver may have a normal imaging appearance at US, CEUS, CT, and MRI. Thus, a normal imaging appearance does not exclude cirrhosis.

Certain morphological, parenchymal, vascular, biliary, and extrahepatic alterations of cirrhosis may be visible at imaging, however. Their recognition alerts the radiologist to the possibility of cirrhosis. In general these features lack perfect specificity and so do not establish the diagnosis of cirrhosis in a clinical vacuum. Radiologists that suspect cirrhosis based only on imaging features should confirm the diagnosis by reviewing the EMR or other means before applying LI-RADS. Alternatively, they can apply LI-RADS conditionally.

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