Hepatic hemangioma

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INTRODUCTION

Hepatic hemangiomas (also referred to as cavernous hemangiomas because of the cavernous vascular space seen histologically) are the most common benign liver lesion. Hepatic hemangiomas are often solitary but multiple lesions may be present. Most patients with hepatic hemangiomas are asymptomatic and have an excellent prognosis, while symptoms are more likely to occur in patients with large lesions.

The etiology of hepatic hemangiomas is incompletely understood. They are thought to be vascular malformations or hamartomas of congenital origin that enlarge by ectasia rather than by hyperplasia or hypertrophy.

This topic will focus on the clinical features, diagnosis, and management of patients with hepatic hemangiomas. The approach to patients with other benign, solid liver lesions is discussed separately. (See "Hepatocellular adenoma" and "Focal nodular hyperplasia".)

The clinical features, diagnosis and management of hepatocellular carcinoma are discussed separately:

- (See "Clinical features and diagnosis of hepatocellular carcinoma".)
- (See "Overview of treatment approaches for hepatocellular carcinoma".)
- (See "Surveillance for hepatocellular carcinoma in adults".)

EPIDEMIOLOGY AND RISK FACTORS

Prevalence — Hepatic hemangiomas are the most common benign liver lesion, with an estimated prevalence of 0.4 to 20 percent in the general population [1-3]. While the highest estimates have been derived from autopsy studies [1,4], there is increasing recognition of hemangiomas in asymptomatic individuals undergoing abdominal imaging for other reasons [5].

Age and sex — Hepatic hemangioma can be diagnosed at any age; however, the majority of lesions (60 to 80 percent) are diagnosed in patients who are between the ages of 30 and 50 years. In adults, hemangiomas occur more frequently in women with a ratio of approximately 3:1 [4,6].

Exposure to estrogens — Hepatic hemangiomas may increase in size during pregnancy or with estrogen therapy; but the exact mechanism of hormonal influence is unclear [7-9]. In a prospective cohort study including 94 women with 181 hemangiomas, patients on estrogen therapy had higher rates of lesion enlargement over time compared with unexposed patients (23 versus 10 percent) [10]. However, estrogen receptors are not present in all hemangiomas, and tumor growth has been demonstrated in the absence of estrogen therapy and in postmenopausal women [11,12].

PATHOLOGIC FEATURES

- Macroscopic features: Hemangiomas are often solitary, but multiple lesions may be present in up to 40 percent of patients [13]. The majority are small (<5 cm), while size ranges from a few millimeters to over 20 cm. Hemangiomas ≥10 cm are referred to as giant hemangiomas. While hemangiomas can be found in both lobes of the liver, they are more frequently located in the right lobe [3].

  On gross examination, hemangiomas appear as well-circumscribed, flat lesions with a dark red-blue color and are often surrounded by a thin capsule [3,14]. The cut surfaces exhibit a red-brown appearance with a spongy consistency that may show hemorrhage, scarring, or calcification (picture 1).

- Microscopic features: Microscopically, the lesion is composed of cavernous vascular spaces of varying sizes, lined by a single layer of flat endothelium and filled with blood [15]. The vascular compartments are separated by thin fibrous septae and may contain thrombi

(picture 2). Giant hemangiomas may develop a collagenous scar or fibrous nodule as thrombosis occurs.

CLINICAL FEATURES

Patient presentation — Hemangiomas are typically discovered incidentally on abdominal imaging or during the work up of abnormal liver biochemical tests. Most patients do not report symptoms.

When symptoms are present, right upper quadrant pain or fullness is common. Less common symptoms include nausea, anorexia, and early satiety, which may develop with large hemangiomas due to compression of adjacent organs [16]. Rarely, acute abdominal pain can result from lesion thrombosis or bleeding that results in stretching and inflammation of the liver capsule [13]. Abdominal pain from an acute thrombosis may be associated with fever and abnormal liver biochemical tests [17]. Other rare presentations include the development of hemobilia following hemangioma rupture into the biliary tree [18].

Symptoms are generally associated with larger hemangiomas (ie, >10 cm) [3].

Physical examination is usually normal, but may reveal a palpable liver or mass. A bruit is rarely heard over the hemangioma.

Laboratory findings — Liver biochemical and function test abnormalities are uncommon but may occur in patients with a complication such as thrombosis, bleeding, or compression of the biliary tree.

Imaging — The imaging appearance of hepatic hemangioma depends on the specific imaging modality (ultrasound, magnetic resonance imaging [MRI], computed tomography [CT] scan), use of contrast enhancement, and multiphasic techniques.

Ultrasound

- **Noncontrast ultrasound** – Noncontrast ultrasound typically reveals a well-demarcated, homogeneous, hyperechoic mass (image 1). In patients with fatty infiltration of the liver, a hemangioma may appear as a hypoechoic mass due to the bright signal from the surrounding parenchyma. Blood flow within the hemangioma can be demonstrated by color Doppler in 10 to 50 percent of hemangiomas [19-22].

- **Contrast-enhanced ultrasound** – Contrast-enhanced ultrasound (CEUS) uses contrast agents to improve visualization by enhancing the ultrasound signal produced by flowing

blood. In hemangiomas, the most common findings on CEUS are peripheral nodular enhancement in the arterial phase, followed by partial or complete centripetal fill-in (image 2) [23]. Enhancement is sustained through the late phase of imaging. CEUS features of liver lesions including hepatic hemangiomas are discussed in more detail separately. (See "Contrast-enhanced ultrasound for the evaluation of liver lesions".)

Cross-sectional imaging

- **Magnetic resonance imaging** – The typical hemangioma appearance on MRI is a smooth, well-demarcated, homogeneous mass that has low signal intensity on T1-weighted images and is hyperintense on T2-weighted images (image 3) [24,25]. If intralesional fibrosis is present, it results in areas of low intensity on T2-weighted images.

  The use of a contrast agent and multiphase technique results in arterial phase enhancement of the lesion's peripheral zone that has variable thickness and may have a corrugated inner margin, while the lesion's center remains hypodense [26,27]. (See "Patient evaluation before gadolinium contrast administration for magnetic resonance imaging".)

- **CT** – On contrast enhanced CT, hemangiomas demonstrate peripheral nodular enhancement in the early phase, followed by a centripetal pattern or "filling in" during the late phase [28,29]. The lesions classically opacify after a delay of three or more minutes and remain isodense or hyperdense on delayed scans (image 4). Possible exceptions are larger hemangiomas, in which the center of the lesion may not opacify completely. Variations in vascular enhancement among hemangiomas may be due to differences in the size of the vascular spaces, the presence of cystic spaces, and the amount of scar tissue within hemangiomas. Absence of enhancement is seen in hemangiomas with large cystic areas or scar tissue [30]. (See 'Pathologic features' above.)

  A noncontrast-enhanced CT scan of a hemangioma usually demonstrates a well-demarcated hypodense mass (image 4). The lesions may appear as hyperdense relative to the surrounding parenchyma in patients with fatty infiltration of the surrounding liver.

DIAGNOSTIC APPROACH

The diagnosis of hepatic hemangioma may be suspected in a patient without cirrhosis who is found to have a solid liver lesion on imaging. The general approach to incidental liver lesions identified by imaging is discussed separately. (See "Approach to the adult patient with an incidental solid liver lesion".)

Hepatic hemangioma is largely a radiographic diagnosis that can be made with noncontrast ultrasound if the following criteria are met [3,31]:

- Typical features are present (ie, homogenous, hyperechoic, well-delineated margin).
- Lesion size is <3 cm.
- Patient has no history of cirrhosis or extrahepatic malignancy [31,32].

If these criteria are not met, the diagnosis is based on contrast-enhanced imaging (eg, MRI, CT scan). We perform contrast-enhanced MRI because it is highly accurate with a sensitivity of approximately 90 percent and a specificity of over 90 percent [24,33,34]. MRI using gadolinium-based contrast and multiphasic enhancement can help differentiate hepatic hemangiomas from other solid liver lesions (eg, hepatocellular carcinoma), and the use of gadolinium-based magnetic resonance contrast agents for evaluating liver lesions is discussed separately [35]. (See "Patient evaluation before gadolinium contrast administration for magnetic resonance imaging" and 'Differential diagnosis' below.)

Patients with a history of cirrhosis or extrahepatic malignancy are at risk for liver malignancy (eg, hepatocellular carcinoma or hepatic metastases, respectively), and such patients require contrast-enhanced imaging to confirm the diagnosis of a benign hemangioma [32]. (See "Clinical features and diagnosis of hepatocellular carcinoma", section on 'Diagnostic approach'.)

We do not perform fine-needle aspiration biopsy (ie, targeted liver biopsy) of a possible hemangioma for the following reasons:

- The availability of imaging with high diagnostic accuracy [24,33,34].
- Risk of rupture or bleeding resulting in hemodynamic instability, need for blood transfusion, or mortality [36-38].
- Low diagnostic yield [39,40]. For example, in a study including 36 patients with suspected hepatic hemangioma who had fine-needle aspiration biopsy, sufficient tissue for making a diagnosis was obtained from 21 patients (58 percent) [38].

DIFFERENTIAL DIAGNOSIS

Solid liver lesions such as hemangiomas are largely a radiologic diagnosis. However, if the imaging characteristics on contrast-enhanced, cross-sectional imaging are not typical, additional evaluation may be required. The differential diagnosis includes:

- **Hepatocellular carcinoma (HCC)** – HCC is a possible cause of a solid liver lesion, particularly for patients with cirrhosis. However, some liver lesions in such patients have imaging features that are not typical for HCC. Serial imaging to document lesion stability or to demonstrate evolving features of HCC is often required in this setting. Imaging criteria for the diagnosis of HCC (Liver Imaging Reporting and Data System) are discussed separately. (See "Clinical features and diagnosis of hepatocellular carcinoma".)

- **Metastatic disease** – Metastases to the liver are a possible cause of a solid liver lesion in patients with a history of extrahepatic malignancy. In such patients, the evaluation should start with imaging to search for metastatic disease in other organs, and this is discussed separately. (See "Approach to the adult patient with an incidental solid liver lesion", section on 'Patients with extrahepatic malignancy'.)

MANAGEMENT

Asymptomatic patients — Asymptomatic patients with hepatic hemangioma do not require treatment, and they are observed for the development of symptoms. The approach to surveillance imaging is based on hemangioma size:

- ≤5 cm: No further imaging

- >5 cm: Contrast-enhanced magnetic resonance imaging (MRI) in 6 to 12 months:

  - If the lesion size remains stable on surveillance imaging (ie, growth rate ≤3 mm per year), no further imaging is performed.

  - If the lesion appears to be growing at a rate >3 mm per year, we repeat surveillance with contrast-enhanced MRI in 6 to 12 months. If the lesion appears stable, no further imaging is performed.

If the lesion continues to grow at a rate of >3 mm per year, the patient is evaluated by a multidisciplinary team (eg, hepatologist, hepatobiliary surgeon) for consideration of surgical intervention. While a specific growth rate and/or maximum lesion size is not a prerequisite for surgical intervention, the decision to intervene is usually based on symptom severity and lesion size. (See 'Symptomatic patients' below.)

Long-term follow-up of hemangiomas demonstrates that most lesions exhibit either slow or no growth and rarely develop complications. (See 'Outcome' below.)

Symptomatic patients — Intervention is rarely needed for patients with hepatic hemangioma. However, patients who have persistent symptoms attributed to the hemangioma (eg, early satiety, abdominal pain) are evaluated by a multidisciplinary team (hepatologist, hepatobiliary surgeon) for consideration of surgical intervention. The decision to intervene is individualized and is typically based on severity of symptoms and lesion size.

However, for patients who have abdominal pain in the absence of additional symptoms (eg, early satiety, nausea), other causes of pain should be excluded prior to intervention. The evaluation of the patient with abdominal pain is discussed separately. (See "Evaluation of the adult with abdominal pain".)

Surgical methods for treating hepatic hemangioma include liver resection or enucleation [41-48]. In addition, for some patients with giant hemangiomas (size >10 cm), preoperative transcatheter arterial embolization has been used to reduce lesion size prior to surgical intervention [49-51]. (See "Overview of hepatic resection" and "Surgical techniques for managing hepatic injury".)

Data suggest that enucleation was associated with better overall outcomes than anatomic liver resection (eg, lobectomy), while the specific approach also depends on surgeon preference and lesion location. In a meta-analysis of nine studies including 1185 patients with hepatic hemangioma, patients who underwent enucleation had a lower risk of postoperative complications (relative risk 0.66, 95% CI 0.52-0.84) and less blood loss compared with patients treated with liver resection [47]. No surgery-related deaths were reported in either group.

Data from observational studies suggest that the majority of symptomatic patients with hemangioma benefit from surgical intervention [41,52-54]. In a multicenter observational study including 204 patients who underwent resection for abdominal symptoms, 129 patients (63 percent) reported symptomatic improvement postoperatively during a 90-day follow-up period [41]. In addition, hepatic resection was associated with low mortality rate (0.8 percent).

SPECIAL POPULATIONS

Pregnancy — We do not advise against pregnancy for asymptomatic female patients with known hepatic hemangioma who wish to conceive; in addition, we do not routinely perform surveillance liver ultrasound during pregnancy [29,55-57]. The risks associated with pregnancy have not been well-defined, although limited data suggest the following:

- Conservative management consisting of observation is associated with good maternal and fetal outcomes. In a case series of four women with hemangiomas (size range: <2 cm to 8

cm) and a total of seven pregnancies, all patients were managed with observation only [57]. No hemangioma growth or complications occurred during gestation or delivery. One year after delivery, one patient had lesion growth to 10 cm that was associated with pain, and she underwent surgical enucleation.

- Estrogen may influence lesion growth, but the risk of lesion rupture is similar for pregnant and nonpregnant women [58]. (See 'Exposure to estrogens' above.)

Children — Hepatic hemangiomas in children most commonly occur in the setting of multiple skin hemangiomas and rarely may be associated with complications such as heart failure. The clinical features and management of infantile hemangiomas are discussed separately. (See "Infantile hemangiomas: Epidemiology, pathogenesis, clinical features, and complications" and "Infantile hemangiomas: Management".)

The management of kaposiform hemangioendothelioma, a rare vascular tumor occurring during infancy or early childhood, is discussed separately. (See "Tufted angioma, kaposiform hemangioendothelioma (KHE), and Kasabach-Merritt phenomenon (KMP)".)

Diffuse hemangiomatosis — Hepatic hemangiomatosis (ie, the presence of hemangiomas throughout the liver), is rare in adult patients [11,59]. The etiology is unknown, although an association with hereditary hemorrhagic telangiectasia has been suggested [60]. (See "Clinical manifestations and diagnosis of hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)", section on 'Hepatic involvement'.)

OUTCOME

Prognosis — The overall prognosis for most patients with hepatic hemangioma is favorable because most lesions remain asymptomatic and without complications [6,61]. In a study including 76 patients with asymptomatic hepatic hemangiomas, none of the patients developed symptoms or complications during a mean follow-up of 92 months [6].

Data suggest that some hepatic hemangiomas will grow over time; however, the clinical significance of the typical growth rate is uncertain [62,63]. In a study including 123 patients with a total of 163 hemangiomas (mean size 3 cm) that were examined with a minimum of two cross-sectional studies at least one year apart, 83 lesions (51 percent) increased in size by any amount, while 74 lesions (45 percent) shrunk and six lesions (4 percent) were unchanged. For lesions that grew, the mean linear growth rate was 3 mm per year [63]. Hemangioma growth resulting in symptoms is uncommon; however, when symptoms do occur, surgical intervention may be required [12,64,65]. (See 'Symptomatic patients' above.)

Complications — Bleeding from a ruptured hemangioma is exceedingly rare [6,66-69], and the risk of rupture does not appear to increase with increasing lesion size [68]. Hemangioma rupture is typically managed with transcatheter arterial embolization of the hepatic artery to control bleeding before proceeding with surgical resection [66,67].

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: Focal liver lesions".)

SUMMARY AND RECOMMENDATIONS

- **Epidemiology** – Hepatic hemangiomas are the most common benign liver lesion, with an estimated prevalence of 0.4 to 20 percent in the general population. In adults, hemangiomas occur more frequently in women, and they can be diagnosed at any age. (See 'Epidemiology and risk factors' above.)

- **Clinical features** – Hemangiomas are typically discovered incidentally on abdominal imaging, and most patients do not report symptoms. When symptoms are present, right upper quadrant pain or fullness is common. (See 'Patient presentation' above.)

- **Diagnostic approach** – Hepatic hemangioma is largely a radiographic diagnosis that can be made with noncontrast ultrasound if the following criteria are met (see 'Diagnostic approach' above):

  - Typical features are present (ie, homogenous, hyperechoic, well-delineated margin)
  - Lesion size is <3 cm
  - Patient has no history of cirrhosis or extrahepatic malignancy

  For patients who not meet these criteria, the diagnosis is based on contrast-enhanced cross-sectional imaging (eg, magnetic resonance imaging (MRI), computed tomography scan).

- **Management** – For asymptomatic patients with hepatic hemangioma, no treatment is required. The approach to monitoring is based on lesion size (see 'Asymptomatic patients' above):

  - Lesions ≤5 cm: No further imaging

- Lesions >5 cm: Surveillance imaging (contrast-enhanced MRI) in 6 to 12 months:
  - If lesion size remains stable (ie, growth rate ≤3 mm per year), no further imaging
  - If the lesion appears to be growing at a rate >3 mm per year, surveillance imaging with contrast-enhanced MRI is repeated in 6 to 12 months. If the lesion appears stable, no further imaging is performed.

If the lesion continues to grow at a rate of >3 mm per year, the patient is evaluated by a multidisciplinary team (eg, hepatologist, hepatobiliary surgeon) for consideration of surgical intervention.

For patients with persistent symptoms attributed to hepatic hemangioma, the patient is evaluated by a multidisciplinary team. The decision to intervene is typically based on symptom severity and lesion size. Surgical approaches include enucleation or liver resection (eg, lobectomy). For giant hemangiomas (>10 cm) and/or those with bleeding, transcatheter arterial embolization to reduce lesion size may be performed prior to elective surgery. (See 'Symptomatic patients' above.)

- **Prognosis** – For most patients with hepatic hemangioma, the prognosis is favorable. Some hemangiomas will grow over time; however the clinical significance of the typically slow growth rate is uncertain. (See 'Outcome' above.)

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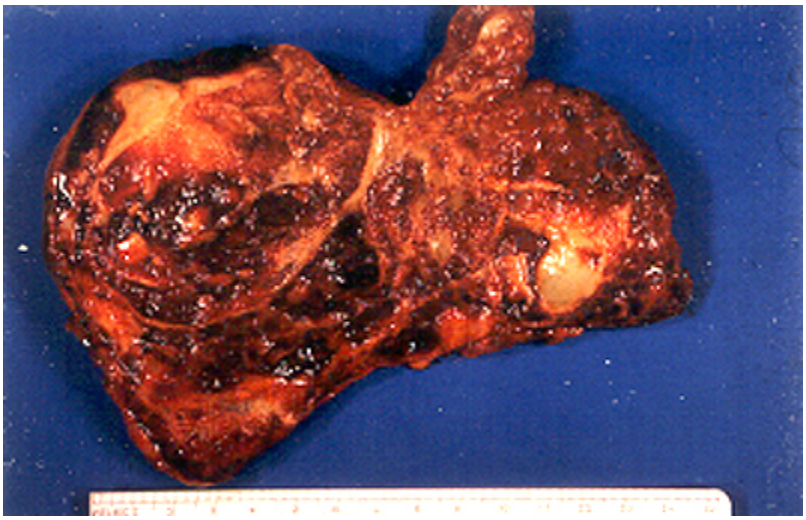
GRAPHICS

Hepatic hemangioma

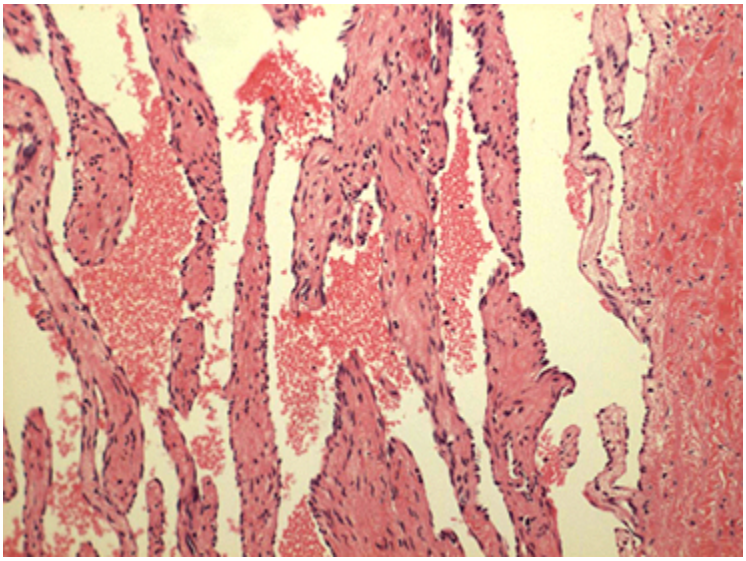


Gross specimen of a hepatic hemangioma. The cut surface demonstrates a brown to red appearance with areas of focal hemorrhage and fibrosis.

Courtesy of Imad Nasser, MD.

Graphic 53994 Version 1.0

Cavernous hepatic hemangioma

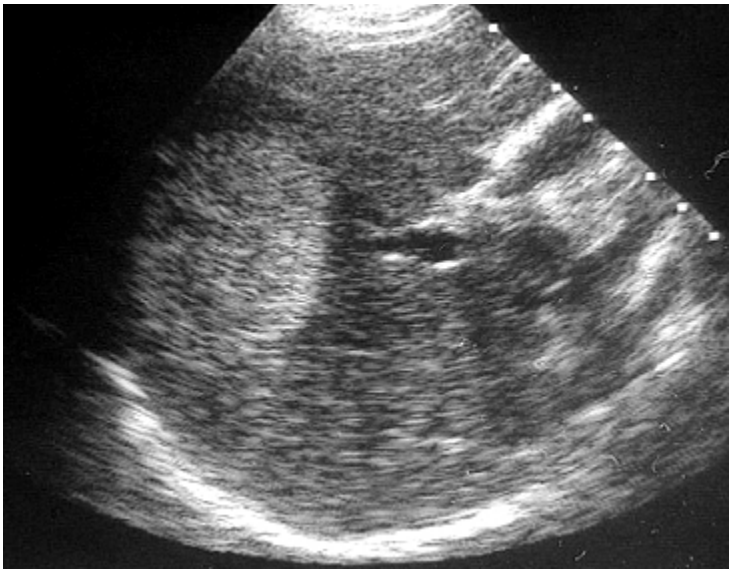


Multiple vascular channels of various sizes lined by a single layer of flattened endothelium and supported by thin fibrous septae (hematoxylin and eosin).

Courtesy of Imad Nasser, MD.

Graphic 65735 Version 2.0

Hepatic hemangioma

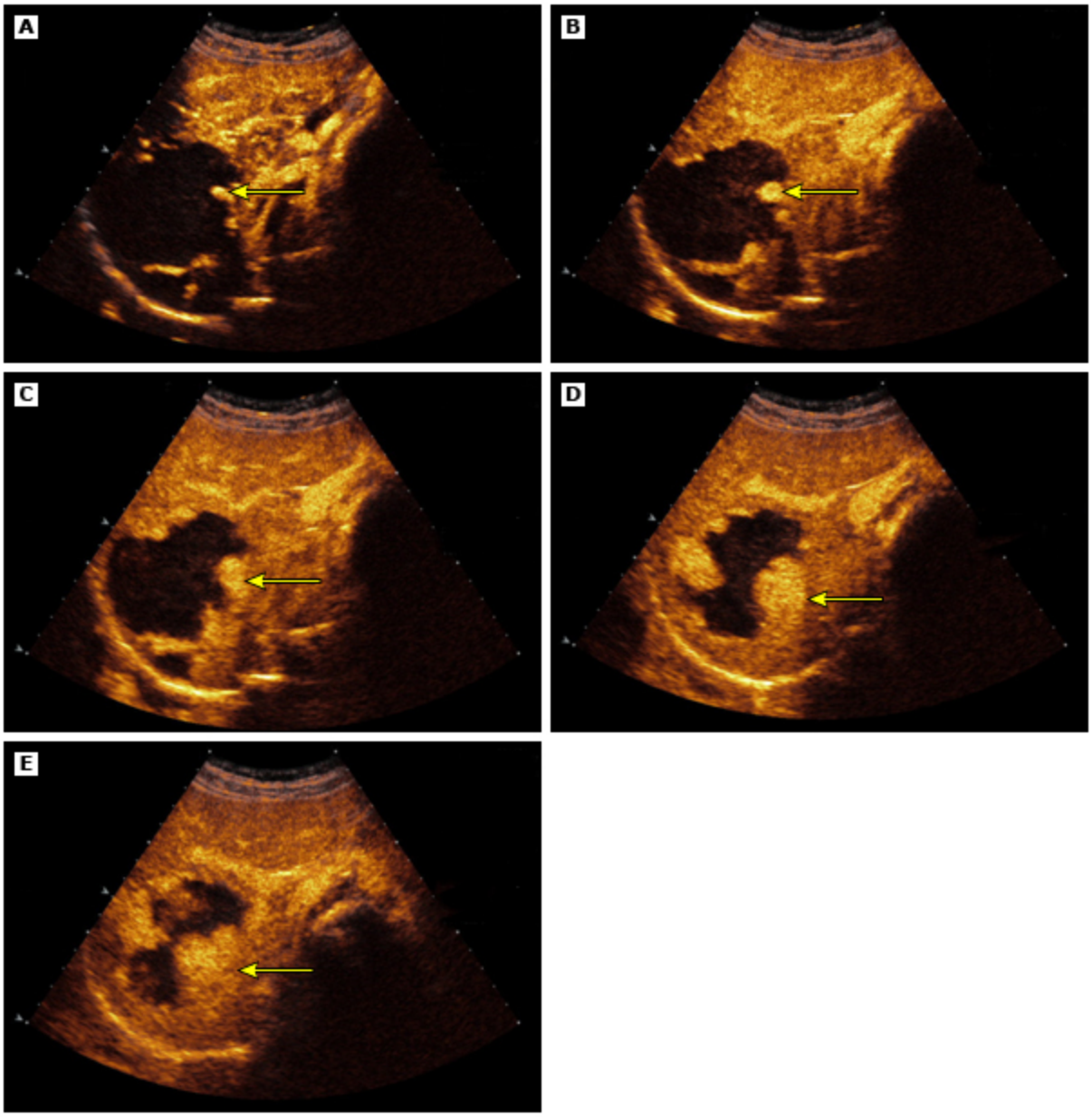


Ultrasound of a hepatic hemangioma shows a homogenous, hyperechoic lesion with an etched border.

Courtesy of Jonathan Kruskal, MD.

Graphic 77575 Version 3.0

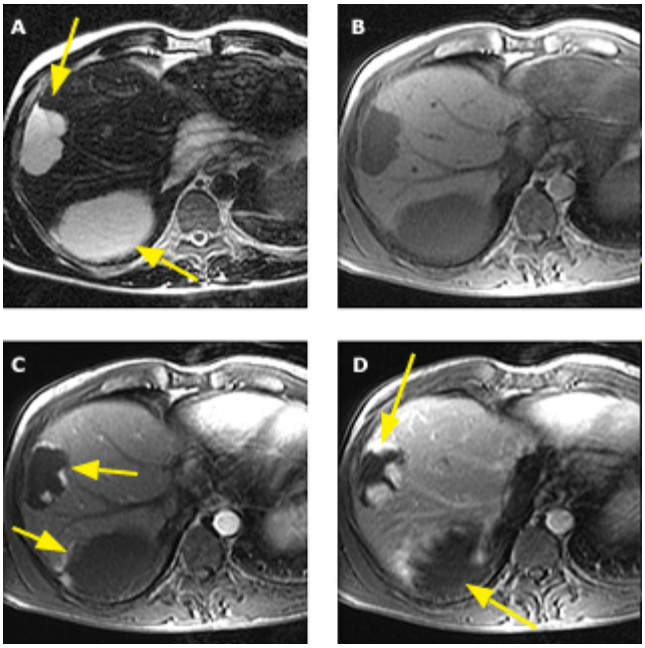
Contrast-enhanced ultrasound of a hepatic hemangioma



The typical contrast-enhanced ultrasound findings in hepatic hemangiomas include peripheral nodular contrast enhancement (A-E) with centripetal fill-in (iris diaphragm phenomenon).

Graphic 96792 Version 2.0

Cavernous hepatic hemangioma

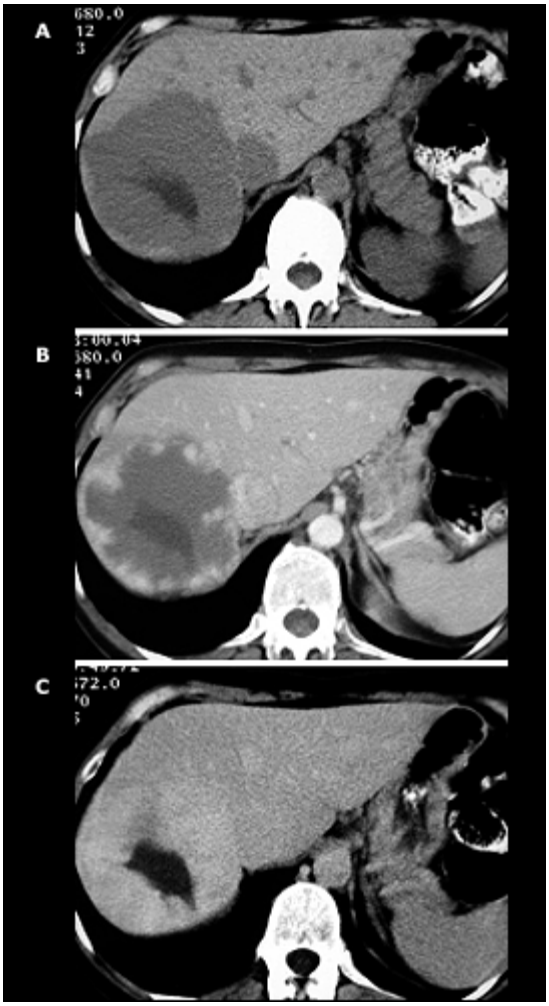


Magnetic resonance (MR) imaging of a cavernous hemangioma in an asymptomatic 52-year-old man. Panel A: Heavily T2-weighted MR image shows the masses (arrows) as very high signal intensity. Panels B-D: Dynamic T1-weighted gradient-echo MR images before (B), during the arterial-phase of gadolinium chelate-enhancement (C), and during the portal phase of enhancement (D) show initial nodular peripheral enhancement (arrowheads) that starts to fill in the hemangiomas (arrows).

Courtesy of Eric Outwater, MD.

Graphic 77870 Version 4.0

Hepatic hemangioma



Dynamic CT scans showing a well-demarcated hypodense lesion on non-contrast scan (panel A) in the posterior right lobe of the liver. Panel B shows early phase of contrast enhancement demonstrating peripheral nodular enhancement with gradual "filling in" of the lesion. The center of the lesion remains hypodense. Panel C shows the post contrast delayed image, which demonstrates an isodense lesion characteristic of hepatic hemangioma.

CT: computed tomography.

Courtesy of Jonathan Kruskal, MD.

Graphic 70560 Version 4.0

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