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Morphometric changes and imaging findings of diffuse liver disease in relation to intrahepatic hemodynamics

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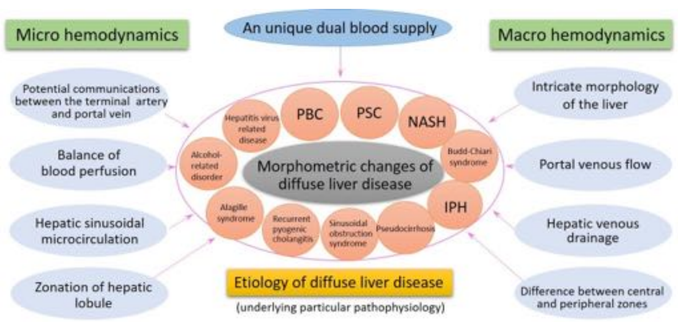
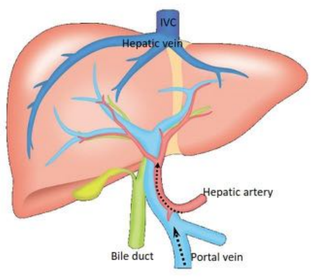


Diffuse hepatic diseases have a variety of etiologies, and any underlying pathophysiologic condition affects the intrahepatic hemodynamics. A temporal disorder of intrahepatic hemodynamics is compensated for by vascular communication, while long-term alteration of the intrahepatic hemodynamics results in an increase in the total hepatic vascular resistance. Blood flow disorders induced by this increased vascular resistance elicit hepatic cellular necrosis and fibrosis, and in the advanced stage, morphometric changes to the whole liver occur due to the combination of selective atrophy and compensatory hypertrophy (atrophy-hypertrophy complex). In addition to the alteration of microhemodynamics, several factors including the specific pathophysiology of each etiology affect the morphometric changes. Each diffuse hepatic disease shows characteristic morphometric changes, and these changes are clearly depicted by CT and MR imaging.

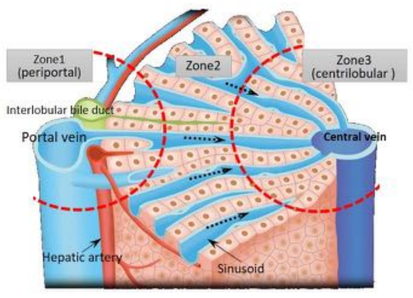
In this presentation, we review each mico- or macro-intrahepatic hemodynamic factor and characteristic imaging findings of morphometric changes and accompanying accessory findings of each etiology.

Blood flow of the liver



The normal liver receives a unique dual blood supply from the hepatic artery (30%) and portal vein (70%).

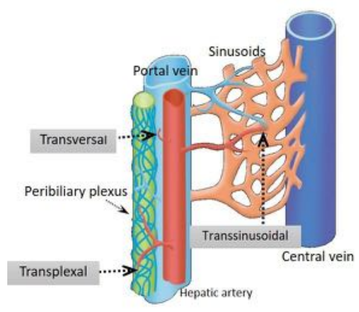
Hepatic lobule and zonation



There is a heterogeneity of hepatocytes with respect to their metabolic activities, resulting in a zonal differentiation of hepatocytes. Which zone will predominantly be affected depends on the etiology.

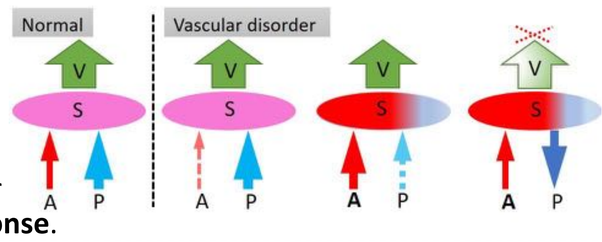
Blood flow from the hepatic artery and portal vein both drain into the hepatic sinusoids, and collect in a central vein that drains into the hepatic vein.

Potential communications



There are several potential communications between the terminal hepatic arterioles and the terminal portal venules, including
- transsinusoidal routes
- transversal routes (vasa vasorum of the portal vein)
- transplexal routes (peribiliary plexus)

When a vascular disorder occurs, these vascular communications play an important role in the balance of blood perfusion to the liver parenchyma.

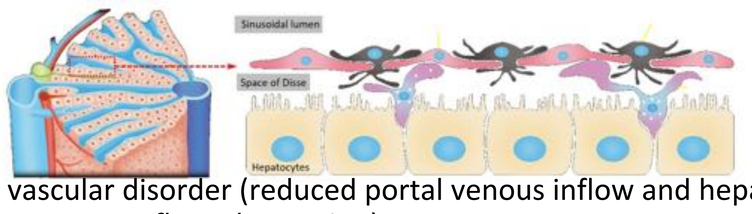


Balance of blood perfusion

Hepatic perfusion disorders can be classified by their pathophysiological mechanisms involving the arterial inflow, portal venous inflow, hepatic sinusoidal microcirculation, and hepatic venous outflow. The response is an important compensatory mechanism to maintain perfusion of the liver parenchyma through an increase of hepatic arterial flow and a reduction of portal venous flow, which is known as the **hepatic arterial buffer response**.

Hepatic sinusoidal microcirculation disorder

The sinusoids are lined with endothelial cells and flanked by plates of hepatocytes. The space between a hepatocyte and a sinusoid is called the space of Disse, and contains hepatic stellate cells. Hepatic sinusoidal microcirculation disorder is elicited by multiple conditions (systemic inflammation, drug intake, etc.) in addition to the aforementioned direct hepatic vascular disorder (reduced portal venous inflow and hepatic venous outflow obstruction).



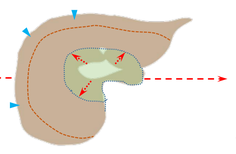
A variety of mediators (such as endotoxins) reach the liver and cause significant alterations in the regulation of blood flow. In the response to liver injury, extensive changes occur in the sinusoids. Endothelin and nitric oxide (NO) are potent vasoconstricting and relaxing agents, respectively, and are mainly related to sinusoidal blood flow. Other factors may also interact with the activation of stellate cells and sinusoidal blood flow.

Asymmetric and complicating morphometrical structures of the liver

Histologically, the hepatic lobule has an identical structure throughout the liver parenchyma. However, non-homogeneous morphometric alternation of the liver occurs due to the intricate morphology of the liver and characteristics of the vascular anatomy.

Central and peripheral zones

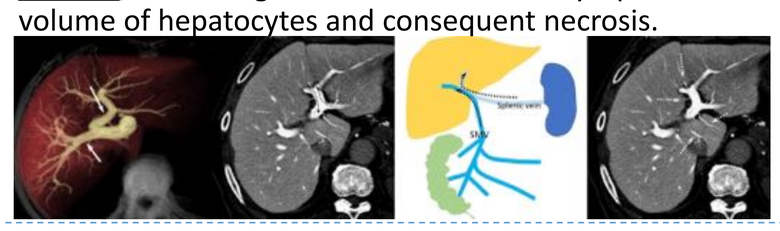
In the area adjacent to the hepatic surface (peripheral zone), the vascular resistance is higher, and the parenchyma can easily become atrophic.



In the area adjacent to the hepatic hilum (central zone), the portal blood flow is preserved through small collaterals, and the hepatic venous drainage is less affected due to the short distance. The area tends to show hypertrophy.

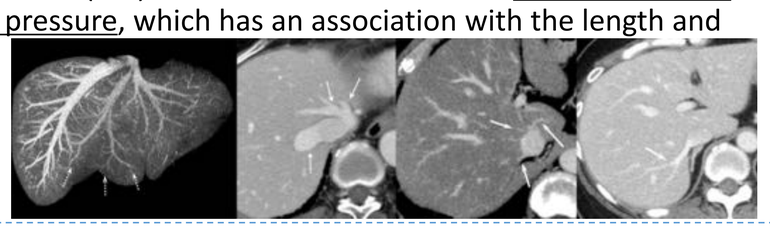
Anatomy and inhomogeneous blood content of portal vein

Several factors influence the portal flow resistance and content, which might result in loss of the cytoplasmic volume of hepatocytes and consequent necrosis.



Asymmetric hepatic venous anatomy and anatomical variation

There are three main hepatic veins, that drain de-oxygenated blood into the inferior vena cava (IVC). Several factors involve the difference of the venous outflow pressure, which has an association with the length and diameter of The hepatic vein and the volume of drainage area.



Atrophy-hypertrophy complex

Any morphometric change is based on the atrophy-hypertrophy complex, which is the controlled restoration following hepatocyte loss. Selective atrophy of the damaged area occurs initially, followed by compensatory hypertrophy of other areas. **Peripheral atrophy and central hypertrophy** are the most significant.

Diffuse hepatic diseases

The parenchymal hepatic diseases presented in this review have been categorized as inflammatory, vascular, bile duct, and deposition-and-storage diseases, depending on the initially-predominant pathophysiologic processes. Liver cirrhosis is the end stage of a wide variety of chronic diffuse liver diseases. In addition, some other conditions can show similar morphological changes to cirrhosis (*).

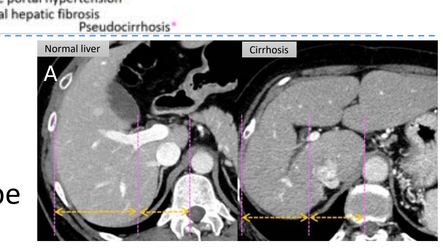
	Zone1 (periportal)	Zone3 (centrilobular)
Inflammatory diseases	Hepatitis virus related disease Sarcoidosis	Alcohol-related disorder Nonalcoholic steatohepatitis Deformity after fulminant hepatitis*
Vascular diseases	Portal venous obstruction* Patent ductus venosus	Congestive heart failure Budd-Chiari syndrome Sinusoidal obstruction syndrome*
Biliary diseases	Primary biliary cholangitis Primary sclerosing cholangitis Recurrent pyogenic cholangitis Alagille syndrome	
Deposition and storage diseases	Iron overload Wilson disease Amyloidosis Glycogen and lipid storage disease	
Others	Idiopathic portal hypertension* Congenital hepatic fibrosis	Pseudocirrhosis*

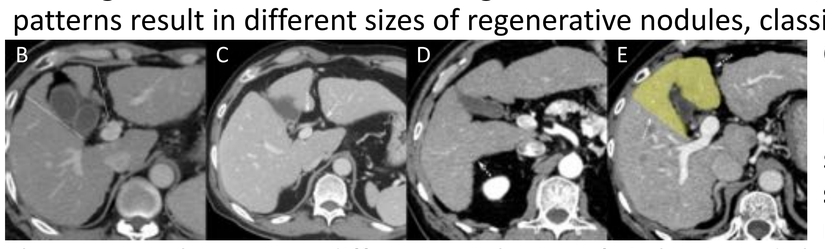
Role of imaging

CT and MR imaging, thus play important roles in the evaluation of diffuse liver disease, offering supporting information on the following factors in a non-invasive manner: configuration of the entire liver, nodular liver surface, regenerative nodules (size), anatomic relationships between the liver and adjacent organs, fibrosis, fat and iron deposits, extrahepatic lesions.

Liver cirrhosis

Cirrhosis is the end-stage disease of various chronic liver diseases, and is pathologically defined as multiple regenerative nodules surrounded by fibrous tissue. Although fibrosis is a common change in chronic liver disease, its histological pattern varies depending on the underlying etiology (Table 1). Different fibrous patterns result in different sizes of regenerative nodules, classified as macro-, micro-, and mixed-nodular cirrhosis based on the size of regenerative nodules.





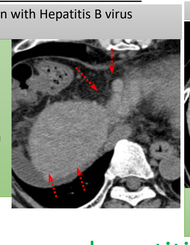
Characteristic morphometric changes of cirrhosis commonly demonstrate atrophy of the right lobe and medial segment and hypertrophy of the caudate lobe and lateral segment. The common morphometric changes of cirrhosis have been expressed in various ways; such as modified **caudate–right lobe ratio** (≧0.55 suggests cirrhosis) [A], **expanded gallbladder fossa** [B], **enlarged periportal space** [C], **right posterior hepatic notch sign** [D], and **selective atrophy of the MHV drainage area** [E]. All of them reflect common characteristic morphometric changes. In addition, nodularity of hepatic surface representing the regenerative nodules is specific for cirrhosis. The patterns of hepatic morphometric changes overlap among different etiologies of cirrhosis and show common tendencies in their appearances, although there are some difference and specificity of each etiology.

Hepatitis virus-related disease

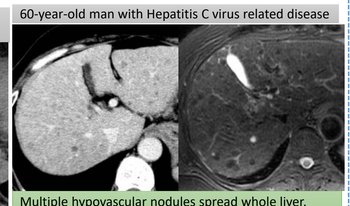
The fibrosis in viral hepatitis and autoimmune hepatitis begin in periportal area (zone 1), eventually leading to macronodular cirrhosis.

60-year-old man with Hepatitis B virus related disease

The nodular liver surface caused by regenerative nodules tends to be distinct in hepatitis B virus-related cirrhosis. (→)



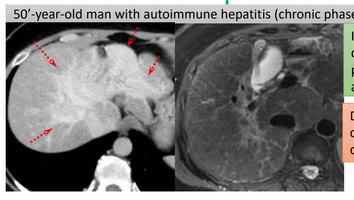
60-year-old man with Hepatitis C virus related disease



Multiple hypovascular nodules spread whole liver, which are regenerative nodules in macronodular cirrhosis.

Autoimmune hepatitis

50'-year-old man with autoimmune hepatitis (chronic phased after acute onset)



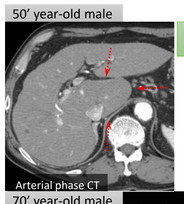
Irregularly atrophy and Non-segmental confluent fibrosis (arrows) are predominantly spread in lateral segment and central area (arrows) .

Dullness of hepatic edge (arrowheads) and central hypertrophy (asterisks) are depicte(↑)

Alcoholic cirrhosis

Fibrosis in alcoholic hepatitis and NASH begins adjacent to the central veins (zone 3), eventually leading to micronodular cirrhosis.

50' year-old male

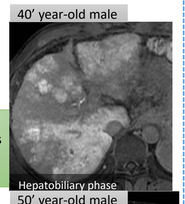


Distinct hypertrophy of the caudate lobe (↓)

Arterial phase CT

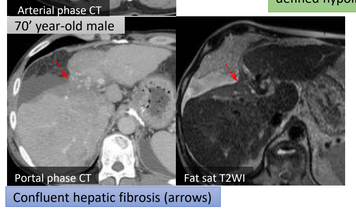
Entire enlargement of the liver due to abundant fibrosis is clearly depicted as ill-defined hypointensity.

40' year-old male



Hepatobiliary phase

70' year-old male

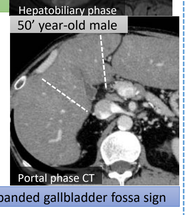


Portal phase CT

Fat sat T2WI

Confluent hepatic fibrosis (arrows)

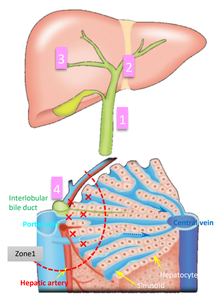
50' year-old male



Portal phase CT

Obscure expanded gallbladder fossa sign

Biliary diseases

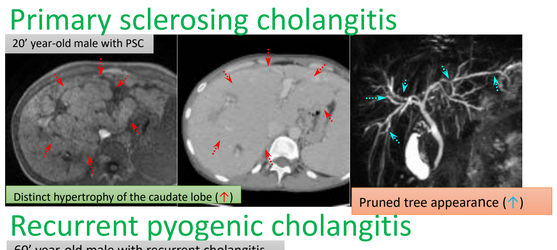


There are several biliary diseases at the following different levels:
1. large intra- and extrahepatic bile ducts (PSC, recurrent pyogenic cholangitis)
2. medium sized bile ducts (PSC, recurrent pyogenic cholangitis)
3. intrahepatic small bile ducts (PBC)
4. interlobular bile ducts (Alagille syndrome)

Although these biliary diseases differ in their clinical and imaging characteristics, they commonly lead to cirrhosis.

Primary sclerosing cholangitis

20' year-old male with PSC

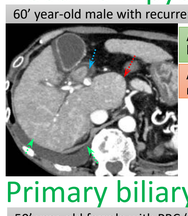


Distinct hypertrophy of the caudate lobe (↑)

Pruned tree appearance (↑)

Recurrent pyogenic cholangitis

60' year-old male with recurrent cholangitis

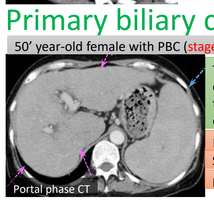


Atrophy of the lateral or posterior hepatic segments, hypertrophy of the caudate lobe (↓)

Arterial phase CT images depict multiple arterioportal shunts, which represent the intrahepatic cholangitis (↓).

Primary biliary cholangitis

50' year-old female with PBC (stage 4) (Child-Pugh class A)



Portal phase CT

The morphometric changes of PBC resemble those seen in other forms of cirrhosis.

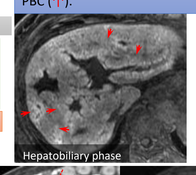
Lymphadenopathy (↑)

Splenomegaly (↑)

Portosystemic shunt

60' year-old female with PBC (stage 4)

Periportal hyperintensity observed can be seen in any diffuse liver disease, but is significantly more prevalent in cases with PBC (↑).



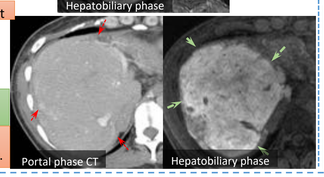
Hepatobiliary phase

Alagille syndrome

40' year-old female

The relatively large portal branch is located in subcapsular area (→)

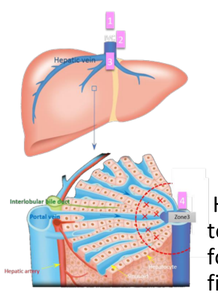
The area of hypertrophy or hyperplasia shows slightly hyperintense compared with the background liver (→).



Portal phase CT

Hepatobiliary phase

Hepatic venous outflow obstruction



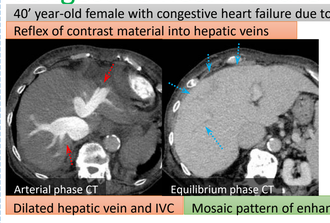
Hepatic venous outflow obstruction can occur at the following levels:
1. the heart (congestive heart failure)
2. IVC (Budd-Chiaris syndrome)
3. hepatic veins (Budd-Chiaris syndrome)
4. sinusoids and central vein (sinusoidal obstruction syndrome)

Hepatic venous outflow obstruction leads to atrophy of hepatocytes in zone 3, following fibrosis. The development of fibrous septa that characteristically bridge the central hepatic veins (reversed lobuli).

Congestive heart failure

40' year-old female with congestive heart failure due to idiopathic pulmonary arterial hypertension

Reflex of contrast material into hepatic veins



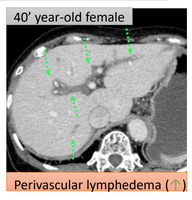
Arterial phase CT

Equilibrium phase CT

Dilated hepatic vein and IVC

Mosaic pattern of enhancement (↑)

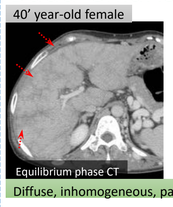
40' year-old female



Perivascular lymphedema (↑)

Budd-Chiaris syndrome

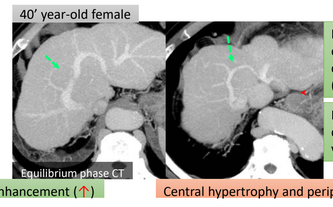
40' year-old female



Equilibrium phase CT

Diffuse, inhomogeneous, patchy enhancement (↑)

40' year-old female



Hypertrophy of the caudate lobe (←)

Intrahepatic collateral veins (↑)

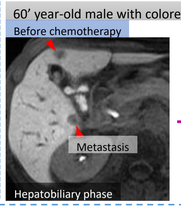
Equilibrium phase CT

Central hypertrophy and peripheral atrophy

Sinusoidal obstruction syndrome

60' year-old male with colorectal hepatic metastasis after 6 cycles of FOLFOX

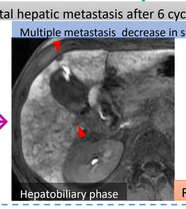
Before chemotherapy



Metastasis

Hepatobiliary phase

Multiple metastasis decrease in size.



Hepatobiliary phase

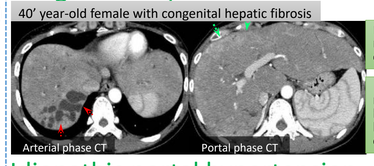
Reticular hypointensity

Noncirrhotic chronic diffuse liver diseases

Several noncirrhotic liver conditions can lead to morphologic changes mimicking cirrhosis.

Congenital hepatic fibrosis

40' year-old female with congenital hepatic fibrosis



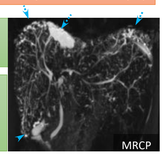
Arterial phase CT

Portal phase CT

Medial segment is normal sized or enlarged (↓)

← Atrophy of the right lobe and hypertrophy of the left lobe and the caudate lobe

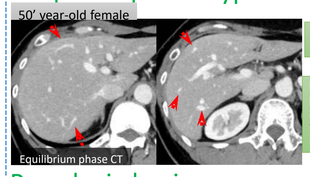
Dilatation of peripheral intrahepatic bile ducts (↓)



MRCP

Idiopathic portal hypertension

50' year-old female

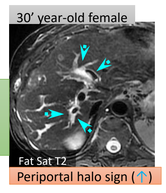


Equilibrium phase CT

Central hypertrophy

Relatively large portal branches are located in the subcapsular area(↑).

30' year-old female



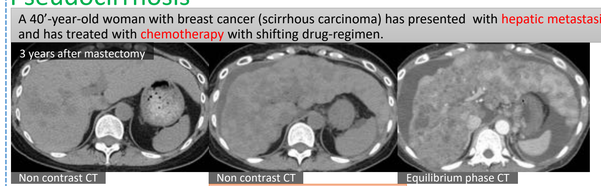
Fat Sat T2

Periportal halo sign (↑)

Pseudocirrhosis

A 40'-year-old woman with breast cancer (scirrhous carcinoma) has presented with hepatic metastasis, and has treated with chemotherapy with shifting drug-regimen.

3 years after mastectomy



Non contrast CT

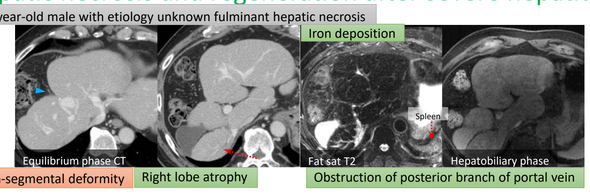
Non contrast CT

Equilibrium phase CT

Deformities mimicking cirrhosis.

Hepatic necrosis and regeneration after severe hepatitis

50'-year-old male with etiology unknown fulminant hepatic necrosis



Equilibrium phase CT

Fat sat T2

Iron deposition

Spleen

Hepatobiliary phase

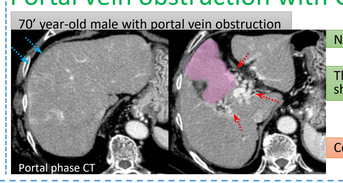
Non-segmental deformity

Right lobe atrophy

Obstruction of posterior branch of portal vein

Portal vein obstruction with Cavernous transformation

70' year-old male with portal vein obstruction



Portal phase CT

Nodularity of hepatic surface is not observed.

The dorsal part of the medial segment does not show atrophy.

Central hypertrophy (↑)

Conclusion

Morphometric changes in diffuse liver diseases are related to several factors including micro-and macro- hemodynamics. Each diffuse hepatic disease shows characteristic morphometric changes that can be clearly depicted by CT and MR imaging.