Hepatic steatosis can occur because of nonalcoholic fatty liver disease (NAFLD), alcoholism, chemotherapy, and metabolic, toxic, and infectious causes. Pediatric hepatic steatosis is also becoming more frequent and can have distinctive features. The most common pattern is diffuse form; however, it can present in heterogenous, focal, multinodular, perilesional, perivascular, subcapsular, and lobar forms. Focal steatosis and fat sparing can occur because of the presence of veins of Sappey, pancreaticoduodenal vein, and aberrant right and left gastric veins, which drain into the liver as third inflow. Hypersteatosis and multinodular forms can mimic metastasis in patients with cancer. Perilesional fat can be seen in insulinoma. Recent introduction of proton-density fat fraction enabled easy and reproducible quantification of hepatic fat. Follow up of patients with NAFLD can be performed for the assessment of treatment response using proton-density fat fraction as biomarker. Multiecho gradient-echo techniques also simultaneously calculate T2* maps, which is important to rule out coexisting hepatic iron overload. NAFLD can progress to steatohepatitis (nonalcoholic steatohepatitis), which can result in cirrhosis. Magnetic resonance (MR) elastography and functional evaluation with Gd-EOB-DTPA are becoming important for monitoring this process. Hepatocellular carcinoma can develop in patients with NAFLD, which is usually a large tumor with necrotic center. In the future, fatty acid maps obtained by MR imaging may allow more detailed analysis of steatosis. MR imaging is superior to ultrasonography and computed tomography for comprehensive evaluation of steatosis.

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**Introduction**

Hepatic steatosis is defined as excessive triglyceride accumulation within the hepatocytes. There are 2 major conditions associated with hepatic steatosis: nonalcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (AFLD). Besides, variable causes such as metabolic, nutritional, drug induced (chemotherapy and steroids), and hepatitis C virus (HCV) infection are listed in the pathogenesis of hepatic steatosis. The natural course of hepatic steatosis varies according to the etiology and accompanied conditions such as inflammation and fibrosis, which has a potential to progress into cirrhosis and liver failure. Therefore, it is important to diagnose and quantify hepatic steatosis. Liver biopsy is the current gold standard for evaluating a patient with suspected hepatic steatosis. However, there are potential drawbacks of liver biopsy such as sampling error, interpretation variability, cost, and associated morbidity. Hence, imaging modalities are commonly used for this purpose. In this article, we review etiology, imaging patterns, and quantification of hepatic steatosis with conventional and advanced imaging techniques.

**Etiology**

Nonalcoholic Fatty Liver Disease

NAFLD is the most common form of hepatic steatosis and affects 30%-40% of men and 15%-20% of women in the general population. It is accepted as hepatic manifestation of metabolic syndrome and has a strong relationship with insulin...
resistance, atherosclerosis, obesity, dyslipidemia, and hypertension. Accumulation of lipids in hepatocytes causes oxidative stress and inflammatory response that leads to nonalcoholic steatohepatitis (NASH), which may progress to cirrhosis. It is estimated that NAFLD would become the most common indication for liver transplantation by 2030.

Alcoholic Fatty Liver Disease
Chronic alcohol intake is another cause of hepatic steatosis, and up to 90% of the alcoholic patients have AFLD. Patients with pure AFLD have a 10% risk of progressing to cirrhosis. Consumption of 30 g ethanol/day was shown to increase the risk of chronic liver damage and cirrhosis in alcoholic patients. Furthermore, female sex, cigarette smoking, obesity, and accompanying hepatic disorders are predisposing factors for liver damage in AFLD.

Metabolic Causes
These factors are divided into 2 main categories: inborn errors of metabolism and acquired metabolic disorders. Inborn errors of metabolism include abetalipoproteinemia, galactosemia, glycogen storage disease, hereditary fructose intolerance, homocystinuria, systemic carnitine deficiency, tyrosinemia, Refsum syndrome, Shwachman syndrome, Weber-Christian syndrome, and Wilson disease. Acquired metabolic disorders are inflammatory bowel disease, jejunoileal bypass, Kwashiorkor and marasmus, starvation and cachexia, and total parenteral nutrition.

Viral Causes
HCV, especially genotype 3, is associated with hepatic steatosis. The prevalence of hepatic steatosis in chronic HCV infection ranges from 40%-80%. The possible mechanisms of hepatic steatosis in HCV infection are direct steatogenic or insulin-resistance effect of HCV viral proteins. Direct steatogenic effect explains hepatic steatosis even in the absence of obesity in patients infected with genotype 3a HCV. Moreover, several viral proteins interfere with insulin signaling, which results with insulin resistance and hepatic steatosis. Hepatic steatosis observed in patients infected with hepatitis B virus is thought to be associated with metabolic factors rather than hepatitis B virus infection.

Drug-Induced Hepatic Steatosis
Hepatic steatosis can be seen as an adverse reaction to some medications such as tetracycline, valproic acid, dexamethasone, amiadarone, methotrexate, tamoxifen, and acetylsalicylic acid. Either microvesicular or macrovesicular steatosis can be observed in drug-induced hepatic steatosis (DIHS). The underlying metabolic syndrome and obesity may aggravate the process of DIHS. It generally occurs with therapy lasting several weeks or months and is reversible after discontinuation. However, some medications should be continued even after the detection of DIHS, such as chemotherapeutic agents, and it is important to monitor the signs of progressive liver damage, which can end up with portal hypertension in these patients (Fig. 1).

Pediatric Hepatic Steatosis
Different factors can be identified in the pathogenesis of hepatic steatosis in children. However, with increasing prevalence, NAFLD is the leading cause of hepatic steatosis in pediatric patients. The other less-common factors of hepatic steatosis are nutritional causes (starvation and malnutrition), intoxications (carbon tetrachloride, organic phosphates, organic solvents, and alcohol), drugs (glucocorticoids, estrogens, tetracyclines, and methotrexate), metabolic disorders, hepatitis C infection, and total parenteral nutrition. NAFLD in pediatric patients is often associated with obesity, insulin resistance, and dyslipidemia.
population is a progressive disease, and 6% of the subjects develop cirrhosis and end-stage liver disease. Therefore, it is important to monitor these patients (Fig. 2).

**Imaging Patterns**

Hepatic steatosis can be seen in different patterns, and being aware of these patterns is important for diagnosis. These include diffuse, focal, perilesional, periporal-perivascular, subcapsular, lobar, and multinodular hepatic steatosis.

**Focal Hepatic Steatosis**

This form of hepatic steatosis occurs mostly because of aberrant hepatopetal venous flow owing to presence of veins of Sappey, pancreaticoduodenal vein, and aberrant right and left gastric veins, which are known as third inflow. It is generally seen as a geographic area within the characteristic locations: gallbladder fossa, subcapsular region, adjacent to the portal vein, or falciform ligament (Fig. 3). Focal steatosis can also be detected as a nodular or masslike lesion, and fat content may not be diagnosed by computed tomography (CT) based on Hounsfield units. In such patients, invisible fat on CT can be diagnosed by magnetic resonance imaging (MRI). Also, typical location, absence of mass effect, and presence of normal vascular structures traversing through the lesion are helpful in differentiating focal hepatic steatosis from other lesions. MRI can be used for ruling out metastasis in patients with cancer who develop new areas of focal fat after chemotherapy. On MRI, characteristic findings are isointensity on in-phase (IP) images and signal drop on out-of-phase T1-weighted images, no diffusion restriction, and isointensity on hepatobiliary phase images. Hypersteatosis is defined as a focal more fatty area in diffuse steatosis and can mimic metastasis in patients with cancer (Fig. 4). Also, intra-voxel or microscopic fat similar to focal steatosis can be present in regenerative nodules, hepatic adenoma, hepatocellular carcinoma (HCC), and rarely in focal nodular hyperplasia.

**Diffuse Hepatic Steatosis**

Diffuse hepatic steatosis is the most common form of hepatic steatosis in which there is a homogeneous fatty appearance in the liver. This form can be seen in all of the etiologic causes of hepatic steatosis. Despite this homogeneous appearance on selected imaging modality, there can be small differences across the liver in quantitative analyses, which would be mentioned in the next section. Also, diffuse heterogeneous form can be seen, and MRI can be used for problem solving (Fig. 5).

**Perilesional, Periportal, and Perivascular Hepatic Steatosis**

Perilesional fat can be seen in patients with insulinoma because of local insulin effect around liver metastases. Fat accumulation can occur in the periporal or perivascular (around hepatic veins) areas, which surrounds portal tracts or hepatic veins with a relative fat sparing in the remainder of the liver.

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**Figure 3** A focal hyperechogenic (arrow) area is seen in segment 4 on US evaluation (A). The same area (arrow) is seen hypodense on CT (B). The diagnosis of focal hepatic steatosis is confirmed with in-phase (C) and out-of-phase (arrow) MR images (D). MR, magnetic resonance.
It was shown that alcoholic cirrhosis, alcohol consumption, and oral corticosteroid therapy may induce perportal-perivascular hepatic steatosis. This entity should be differentiated from other perivascular pathologies such as edema, hemorrhage, extramedullary hematopoiesis, fibrosis, perfusion abnormalities, and neoplasia such as neurofibroma and lymphoma, which have a similar appearance.

Subcapsular Hepatic Steatosis

Subcapsular fatty infiltration is commonly seen in patients who received intraperitoneal insulin within their peritoneal dialysate. High concentration of insulin causes local fat accumulation in the subcapsular zone. This form can be nodular in shape or involves subcapsular region like a rind. This form of hepatic steatosis can also be idiopathic.

Multinodular Hepatic Steatosis

Hepatic steatosis can be detected as multiple nodular or ovoid fat foci throughout the liver. This form is more frequently seen in patients with cancer after chemotherapy, either as new lesions or at the location of metastatic lesions most likely owing to fatty necrosis (Fig. 5). These foci may mimic multiple metastases, which is extremely problematic in patients with known malignancy. The other pathologies that have similar appearances are lymphoma, sarcoidosis, abscesses, candidiasis, and biliary hamartomas. MRI should be used in such patients for differential diagnosis before biopsy.

Lobar Hepatic Steatosis

Lobar fat accumulation is a rare entity that originates from occlusion of right or left portal vein. The reason is thought to be decreased nutrient supply to 1 lobe that results in fat deposition differences between 2 lobes. Diagnosis of lobar hepatic steatosis can be difficult on ultrasound (US) or CT imaging. However, signal drop on out-of-phase images relative to IP images on the effected lobe on MRI is diagnostic (Fig. 6).
appear hypodense at unenhanced CT scan and hypodense or hyperdense on enhanced CT scan. On MRI, it is detected as hypointense area on T1-weighted and hyperintense on T2-weighted images owing to edema. The borders of this area are straight with no anatomical congruity. Findings usually regress in 4-6 months, and irradiated area gradually shrinks with a compensatory hypertrophy in the remaining part of the liver (Fig. 6).

**Metastasis**
Liver metastasis generally appears hypodense on CT, which may mimic hepatic steatosis foci as mentioned in the previous section (Fig. 6). Furthermore, some metastases contain fat as they originate from fat-containing primary tumors such as teratoma, liposarcoma, Wilms tumor, and renal cell carcinoma, which should be kept in mind in oncologic patients. Metastasis in a diffusely fatty liver, which is commonly seen in patients receiving chemotherapy, may not be easily detected on US and CT scans. In such patients, MRI should be preferred for follow-up.

**Fibrosis**
Confluent hepatic fibrosis is seen as a wedge-shaped area with capsular retraction and usually involves segment 4, anterior segment of right lobe, or both in patients with cirrhosis. It is detected as a hypodense area on unenhanced CT and becomes isodense or slightly hypodense on contrast-enhanced CT. These areas can enhance on delayed phase images on CT and MRI.

**Perfusion**
Liver has dual blood supply through the hepatic artery and portal vein. Despite adaptation mechanisms, decreased flow in one of them may lead to perfusion changes in the liver. In case of a portal venous compromise such as thrombosis or compression, perfusion differences causing attenuation differences are detected. The corresponding parenchyma, which can be lobar or focal according to the affected portal vein segment, appears as a hypoattenuating area on arterial phase images. This area can also be detected on unenhanced CT images if it has a long duration. Similar findings can be observed in hepatic venous occlusions or arterioportal shunts as portal vein undertakes the drainage task. Occlusion of hepatic artery alone does not create a meaningful perfusion difference. However, a hypoattenuating area can be identified near a hypervascular tumor because of “steal phenomenon.” In all perfusion abnormalities, dynamic contrast-enhanced CT scans demonstrate phase-dependent attenuation differences in the liver and support the diagnosis (Fig. 6).
Quantification of Steatosis

Quantification of hepatic steatosis is an important issue as it gives information about severity of the disease. The main way to quantify hepatic steatosis is liver biopsy. However, there are potential drawbacks of liver biopsy, and it is not feasible to evaluate patients with liver biopsy in every follow-up period. Hence, imaging modalities are commonly used for this purpose.

Ultrasound

US is an initial screening tool for assessing hepatic steatosis as it is inexpensive and widely available. Hepatic steatosis is detected as increased echogenicity because of increased parenchymal reflectivity on US imaging. Normal liver echogenicity should be equal or slightly more than kidney or spleen parenchyma. Mild hepatic steatosis refers to increased echogenicity and increased discrepancy of echo amplitude between liver and kidney or spleen. Moderate hepatic steatosis can be identified with loss of echoes from the walls of the portal system and severe hepatic steatosis with posterior attenuation.

This technique is highly depended on the examiner and does not provide quantitative information that may be reproducible. Besides, reported sensitivity and specificity values of US to detect hepatic steatosis are variable. Several studies investigated the accuracy of some advanced US techniques for quantification of hepatic steatosis. Despite reported accuracy values, these techniques have limited clinical use for quantification of hepatic steatosis as being complex or based on noncommercial software. Son et al recently described the use of acoustic structure quantification method that is used for the evaluation of diffuse liver diseases in hepatic steatosis assessment, and they observed that focal disturbance ratio measured with acoustic structure quantification has a strong correlation with hepatic fat fraction measured with magnetic resonance spectroscopy (MRS) in this pilot study.

Computed Tomography

Hepatic steatosis leads to reduction of HU value on CT. It is shown that the degree of hepatic steatosis is associated with degree of decrease in attenuation values. There are 2 main methods in estimation of hepatic steatosis with CT, that are, hepatic measurement only and normalization of hepatic attenuation with splenic attenuation. In the first one, hepatic attenuation value can be obtained by placing one or more round of interests (ROIs) in the interested liver parenchyma. In the second one, calculation of spleen-to-liver attenuation ratio or difference between liver and spleen attenuation values can be used for estimation of hepatic steatosis degree.

Expected attenuation value of healthy liver is approximately 50-57 and 8-10 HU higher than the attenuation of spleen. Park et al investigated diagnostic accuracy of hepatic attenuation value, liver-to-spleen attenuation ratio, and the difference of liver and spleen attenuation value for the diagnosis of macrovesicular steatosis of 30% or higher on unenhanced CT images; they observed the highest specificity (100%) for 42 HU, 0.8 and -9 HU, respectively, with no diagnostic superiority among them. A recent study, which used liver-to-spleen attenuation ratio, showed that a ratio of 0.9 discriminated 30% or more hepatic steatosis with a sensitivity of 79% and a specificity of 97%. Kodama et al evaluated hepatic measurement only and comparison of liver attenuation with spleen on both unenhanced and portal phase contrast-enhanced CT images. They found that association of all measurements with pathologic fat content is statistically significant. However, only hepatic measurement was observed as the best for prediction of pathologic fat content, and a value of 40 HU is predictable for 30% hepatic steatosis. Dual-energy CT is promising for the evaluation of hepatic steatosis, which should be verified with further clinical studies. Despite satisfactory sensitivity and specificity values observed in evaluation of hepatic steatosis with CT, radiation exposure limits the usage in children and follow-up evaluation. Besides, it was shown that attenuation values vary with manufacturer and generation of the scanner, which decreases the reliability of CT in quantification of hepatic steatosis.

Magnetic Resonance Imaging

MRI is commonly used in the evaluation of hepatic steatosis as being a noninvasive, nonhazardous, and cross-sectional imaging technique. The principle of MRI to detect and quantify fat mainly depends on chemical-shift effect, which can be defined as the difference of resonance frequencies between hydrogen protons bound to triglycerides and water. This difference can directly be seen on the spectra in MRS or can be calculated with different MRI techniques.

Figure 7 Proton-density fat fraction MR images of patients with 10% (mild) (A), 25% (moderate) (B), and 50% (severe) (C) hepatic steatosis. MR, magnetic resonance.
Magnetic Resonance Spectroscopy

MRS displays molecular composition of the interested tissue as resonance peaks at different locations on the spectra. On MRS spectra of the liver, there are 2 main peaks: water positioned at 4.7 ppm and fat positioned at 1.3 ppm. There are also other identifiable small fat peaks at various locations on the spectra. The signal intensities of these peaks can be quantified by spectral tracing of the peaks, and fat content can be calculated by giving the ratio of signal intensities of fat peaks to the sum of fat and water peaks. MRS of the liver can be successfully performed in a single acquisition with single breath hold. Single-voxel spectroscopy is commonly preferred tool for quantification of fat in the liver, which can be acquired with stimulated echo acquisition mode or a point-resolved spectroscopy sequence. Stimulated echo acquisition mode is accepted as a better sequence for fat quantification as it is less susceptible to J-coupling effects despite a higher signal-to-noise ratio observed in point-resolved spectroscopy sequence. In single-voxel spectroscopy, data are collected from a single voxel, which is placed on the interested liver parenchyma avoiding vessels, bile ducts, and surrounding adipose tissue.

The first study by Longo et al. showed good correlation between MRS and histology-determined hepatic steatosis, and following studies supported this finding. High intra-individual reproducibility was also observed in repeated measurements in the MRS. Therefore, MRS was accepted as a reference imaging method for assessment of hepatic steatosis. However, MRS demonstrates fat fraction of a limited portion of the liver, is not available on all clinical scanners, and requires postprocessing software and specific analyses by a physicist, which limits the usage of the technique as a daily routine. These factors accelerated development of other MRI techniques in the use of quantification of hepatic steatosis.

Magnetic Resonance Techniques

Hepatic steatosis can be detected as increased hepatic signal intensity on conventional T1-weighted magnetic resonance images. However, quantification of hepatic fat is feasible with specific MRI techniques including chemical-shift imaging (CSI) and fat-suppressed imaging approaches. Fat-suppressed imaging techniques use the effect of fat-suppression pulses to observe a decrease in hepatic steatosis and by the way detect fat-containing liver. CSI separates the signals into water and fat by using a similar principle with MRS: the chemical shift-induced signal interference between the protons in fat and water. Net magnetization vectors of protons of fat...
(methylene) and water are positioned in IP (water + fat) and opposed phase (water − fat) depending on the chosen echo time. By the way, fat fraction of the interested tissue can be calculated by measuring the signal intensities on IP and opposed phase images.

This approach was first introduced by Dixon \(^{65}\) and has been improved in recent years. Despite a wide clinical usage of the basic CSI technique, it is prone to biases from T1 and T2* relaxation that may lead to inaccurate fat quantification. Further techniques aimed to minimize these factors by using low flip angle and multiple echo acquisition. Recently, Reeder et al\(^{66}\) defined a complex CSI-based technique called iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL), which is capable to measure proton-density fat fraction (PDFF) of the liver by separating the signals from water and fat with echo asymmetry and least-squares estimation (IDEAL), which is capable to measure proton-density fat fraction (PDFF) of the liver by separating the signals from water and fat. Clinical studies using this technique showed a close correlation between histology-determined steatosis and MRI-PDFF–determined steatosis with high accuracy rates, and currently this method (IDEAL-IQ, Liver-Quant, and m4ixon-Quant) is commercially available by all vendors under different names\(^{57,69}\) (Fig. 7). Moreover, following studies demonstrated that the technique can also be used for quantification of longitudinal changes in hepatic fat content in patients with NAFLD\(^{70,71}\) (Fig. 8).

The studies comparing MRI-PDFF with MRS-determined hepatic steatosis demonstrated an excellent correlation\(^{72,73}\). A recent study observed a good correlation between MRI- and MRS-determined hepatic steatosis in comparison with histology-determined hepatic steatosis with no superiority among them.\(^{74}\) However, it was shown that there can be significant fat distribution differences among different regions of the liver, which is a limitation for MRS.\(^{62}\) MRI-PDFF allows assessment of the whole liver in less than 20 seconds without a specialized physicist to calculate fat fraction and therefore becomes a better approach for quantification of hepatic steatosis. Moreover, iron content of the liver can be determined by T2* maps obtained simultaneously, and therefore opposing effects of fat and iron can be solved by using the same multiecho gradient-echo sequence for PDFF calculation\(^{75}\) (Fig. 9). Recently, feasibility of fatty acid maps has also been reported, which may enable detailed analysis of hepatic steatosis.\(^{76}\)

NAFLD can progress into steatohepatitis (NASH), which can result in cirrhosis. The pathologic findings of NASH include inflammation and various degrees of fibrosis besides steatosis. Therefore, new imaging techniques aim to demonstrate these associated features. Magnetic resonance elastography and functional evaluation with Gd-EOB-DTPA are becoming important for monitoring this process.\(^{77,80}\) It was shown that hepatobiliary phase enhancement ratio showed significant association with steatohepatitis and fibrosis stage in patients with NAFLD (Fig. 10).\(^{77}\) The accuracy of magnetic resonance elastography for staging liver fibrosis was also shown in different studies.\(^{78-80}\) HCC can also develop in

\[\text{Figure 10} \quad \text{Axial MRI at hepatobiliary phase after Gd-EOB-DTPA administration shows decreased enhancement (relative enhancement ratio of 0.7) consistent with decreased function (consistent with steatohepatitis or fibrosis) owing to nonalcoholic fatty liver disease.}\]

\[\text{Figure 11} \quad \text{A large hepatocellular carcinoma is shown on in-phase (A) and out-of-phase MR images (B) in a patient with nonalcoholic fatty liver disease. Capsule, washout, and nonenhancing necrotic area (arrow) can be clearly identified on postcontrast T1-W image (C). Tumor was hypervascular on arterial phase image. MR, magnetic resonance.}\]
patients with NAFLD, which is usually a large tumor with necrotic center (Fig. 11). It is important to identify an HCC in a fatty liver as up to 25% of the patient with NASH can progress to HCC. Moreover, cardiovascular disease associated with NAFLD can be assessed by coronary CT angiography and by measuring liver density on noncontrast CT slices obtained for calcium scoring.

**Conclusions**

There are various etiologic causes and imaging patterns of hepatic steatosis, which are important for radiologic diagnosis. In patients with cancer, some forms of steatosis can mimic metastasis; therefore, in patients with equivocal findings on ultrasonography and CT, MRI should be performed for differential diagnosis. Quantification of hepatic steatosis beyond detection is feasible, and PDFF is becoming a biomarker for follow-up of patients with NAFLD. In the future, fatty acid maps may allow more detailed analysis of steatosis.

**References**


