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Liver Function Assessment by Magnetic Resonance Imaging

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Liver function assessment by hepatocyte-specific contrast-enhanced magnetic resonance imaging is becoming a new biomarker. Liver function can be assessed by T1 mapping (reduction rate) and signal intensity measurement (relative enhancement ratio) before and after GD-EOB-DTPA (gadoxetic acid) administration, as alternative to Tc-99m galactosyl serum albumin scintigraphy, 99m Tc-labeled mebrofenin scintigraphy, and indocyanine green clearance test. Magnetic resonance imaging assessment of liver function can enable diagnosis of cirrhosis, nonalcoholic fatty liver disease associated fibrosis and steatohepatitis, primary sclerosing cholangitis, toxic hepatitis, and chemotherapy and radiotherapy-related changes, which may be only visible on hepatobiliary phase images. Simple visual assessment of signal intensity at hepatobiliary phase images is important for the diagnosis of different patterns of liver dysfunction including diffuse, lobar, segmental, and subsegmental forms. Furthermore, preoperative assessment of liver function is feasible before oncologic hepatic surgery, which may be important to prevent posthepatectomy liver failure and to estimate future remnant volume. Functional magnetic resonance cholangiography obtained by T1-weighted images at hepatobiliary phase can allow diagnosis of acalculous cholecystitis, biliary leakage, bile reflux to the stomach, sphincter of oddi dysfunction, and lesions with communication to biliary tree. Functional information can be easily obtained when Gd-EOB-DTPA is used for liver magnetic resonance imaging.

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Introduction

Advances in liver imaging, particularly in oncology, has resulted in increased number of patients diagnosed at early stage of the disease, and as a consequence more patients may benefit from oncological surgery compared to past. There is also great interest in the management of chronic liver diseases (CLDs) as well. Therefore, assessment of liver function by magnetic resonance imaging (MRI) is gaining importance in oncological and nononcological conditions.

It is important to be able to predict liver function particularly in patients who would undergo surgery for a liver tumor or patients with chronic or acute liver diseases. After large liver volume resection, patients may suffer from postoperative remnant liver failure.[1,2] Thus, accurate estimation of the hepatic functional reserve is fundamental in these patients. Moreover, liver function assessment is also important in the management of patients with CLDs or cirrhosis.[3,4] On the contrary, pseudocirrhotic appearance may be observed in patients suffering from cancer because of liver metastases or as a complication of systemic chemotherapy.[5-7] Revealing normal liver function by imaging may help to diagnose pseudocirrhosis in patients without a history of CLDs.

In this review article, we focus on MRI-based liver function estimation methods in various conditions. We also discuss clinical applications of liver function assessment in liver imaging.

Methods for Noninvasive Estimation of Liver Function

There are several methods used for noninvasive prediction of liver functional reserve in clinical practice. Blood parameters are the basic and daily used methods to evaluate the liver

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function. Standard blood parameters include serum levels of albumin, bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transpeptidase, and prothrombin time. However, estimation of liver function based solely on standard quantitative blood tests is limited.[4,8,9] Nevertheless, there are 2 main scoring systems to overcome individual drawbacks of quantitative blood tests in evaluating liver function. Model for end-stage liver disease (MELD) scoring system uses serum levels of bilirubin, creatinine, and INR. On the contrary, Child-Pugh system includes serum levels of albumin, bilirubin, prothrombin time, presence of ascites, and encephalopathy to predict global liver function.[4,10] Although Child-Pugh and MELD scoring systems are postulated to be more accurate than any other individual blood test, information about liver function is not precisely related to hepatocyte function. However, methods such as Technetium-99m galactosyl serum albumin (99mTc-GSA) scintigraphy, 99m Tc-labeled mebrofenin scintigraphy, and indocyanine green (ICG) clearance test are directly associated with hepatocytes.[11-14] 99mTc-GSA is an analogue of asialoglycoprotein that binds to asialoglycoprotein receptor (present only in mammalian hepatocyte membranes).[11,12,15] Consequently, 99mTc-GSA scintigraphy can measure the distribution and concentration of normal hepatocytes. However, any hepatocyte with an intact membrane may give signal, as 99mTc-GSA does not undergo uptake and excretion process.[11,12,15] 99m Tc-mebrofenin is taken up by hepatocytes via organic anion transport protein (OATP) and subsequently excreted into the biliary tree by multidrug-resistance protein.[13] However, despite additional cost and radiation exposure, liver scintigraphy suffers from limited spatial resolution. On the contrary, ICG clearance test is radiation-free and consists of 2 blood sampling (before and 15 minutes after injection).[11,12] ICG is taken up by hepatocytes via OATP1B1 and excreted into biliary system by multidrug-resistance protein 2 (MDRP2), thus ICG clearance test provides information about uptake and excretion functions of the liver similar to 99m Tc-mebrofenin scintigraphy.[11,12,16] However, ICG clearance test does not provide anatomical detail; furthermore, biliary excreted content cannot be used for additional information about the biliary system.

Gadobenate dimeglumine (Gd-BOPTA) and gadoxetic acid (Gd-EOB-DTPA) are routinely used hepatobiliary-specific agents for MRI. Gd-BOPTA and Gd-EOB-DTPA initially behave as extracellular contrast agents and then both are taken up by hepatocytes and excreted into biliary system. Biliary excretion rate of Gd-EOB-DTPA is markedly higher than Gd-BOPTA with an approximate percentage of 50% and 5%, respectively.[17,18] Therefore, Gd-EOB-DTPA is more suitable for evaluating liver function. Hepatobiliary-specific agents are taken into hepatocytes by active carriers located at the sinusoidal membrane (OATP1B1/B3), and subsequently excreted into the biliary system by MDRP2 without any metabolic change.[4,8,19-21] Because of T1-shortening effect, liver parenchyma with functional hepatocytes exhibits increased signal intensity on T1-weighted magnetic resonance (MR) images. Therefore, decreased or late liver enhancement may be associated with hepatic dysfunction or failure. Besides functional imaging, MRI also demonstrates liver segmental anatomy, vascular patency, and focal lesions as one stop shop technique within 20 minutes. Another strength of functional MRI over other tests is that the excretion of contrast material enables visualization of biliary tree.[17,22-24] Thus, anatomical and functional information about biliary system can also be achieved on postcontrast T1-weighted images or so-called functional MR cholangiography (fMRC).[17,22-24]

Although liver signal intensity measurement is a useful method to estimate liver function, it is known that MRI signal intensity is not an absolute value and may be affected by several technical parameters.[25-28] Signal intensity measurements on MRI images are not similar to Hounsfield unit measurements on computed tomography (CT). Ideally, quantitative evaluation should not rely on enhancement changes before and after contrast enhancement, as there is no direct proportional relationship, and MR signal intensity does not demonstrate a linear straightforward relationship with the gadolinium concentration.[25,27] This issue particularly affects follow-up scans, as detected signal intensity changes between 2 scans can be related to nondisease conditions such as radiofrequency amplifier, repetition time, and echo time, or can be due to disease progression or regression. Nevertheless, researchers have used several methods (eg, relative liver enhancement [RLE] and signal intensity adjustment with spleen, erector spinae muscle, or spinal cord) to predict liver functional reserve by using signal intensity measurements and reported significant correlation.[8,11,29,30]

On the contrary, T1 mapping is an absolute and more reliable value than simple signal intensity measurement.[25-27] Furthermore, reduction rate (RR) of T1 relaxation time before and after contrast enhancement is directly proportional to quantity of accumulated contrast agent in hepatocytes (Fig. 1).[25-27] However, it should be kept in mind that accumulation of copper, iron, manganese, and presence of inflammation may influence basic T1 values of the liver; therefore, using only precontrast T1 relaxation maps per se cannot be trustworthy for evaluating liver fibrosis or function.[31,32]

On the contrary, magnetic resonance elastography is also found to be accurate for estimation of liver functional reserve.[33] However, magnetic resonance elastography requires additional hardware and software that is an obstacle for general use. Diffusion-weighted imaging has been tested as predictor of liver function, yet diffusion-weighted imaging was found to be unreliable.[25,34]

Clinical Applications

In the clinical perspective of imaging-based liver function assessment, the common approach is to discriminate patients with poor liver functional reserve and to diagnose liver dysfunction. However, in patients who are candidates for liver surgery, it is more important to evaluate liver functional reserve for prediction of future residual liver volume.