Quantitative Biomarkers of Diffuse Liver Disease

Fibrosis: Magnetic Resonance Elastography (MRE) & Diffusion-weighted imaging (DWI)

Sudhakar Kundapur Venkatesh, MD, FRCR
venkatesh.sudhakar@mayo.edu
Mayo Clinic, Rochester, MN, USA

Highlights:

- MRE can detect and stage liver fibrosis accurately
- DWI is useful in detection of advanced fibrosis and cirrhosis.
- Newer clinical indications continue to emerge for MRE in the management of chronic liver diseases.

Target audience: Radiologists, radiology residents and fellows, MR technologists interested in the quantitative markers of diffuse liver disease and liver fibrosis.

Background

Chronic liver diseases irrespective of etiology causes liver parenchymal loss and fibrosis. Continued liver damage and untreated liver fibrosis and leads to cirrhosis and its associated complications. Prognosis and management of chronic liver diseases greatly depend on the amount and progression of liver fibrosis. There is renewed interest in early detection and staging of liver fibrosis as antifibrotic drugs are available that can potentially decrease the degree of fibrosis leading to regression of the fibrosis and in the future there is potential for possible reversal of fibrosis.

Evaluation of liver fibrosis needs some kind of quantification. Liver biopsy, the current gold standard for detection and staging of liver fibrosis is not an ideal test as it is invasive, limited by sampling errors, semi-qualitative assessment, low inter observer agreement and has poor acceptance for repeated biopsies. Non-invasive tests are therefore required. Serum tests are good for differentiation of advanced fibrosis from normal but not accurate for detection of early fibrosis. The effectiveness of therapeutic drugs cannot be adequately assessed with serum tests and liver biopsy. Imaging tests are therefore being developed to non-invasively assess liver fibrosis. Among the imaging modalities, MRI offers several techniques to evaluate liver fibrosis including diffusion weighted imaging (DWI), magnetic resonance elastography (MRE), perfusion imaging and MR spectroscopy. MRE and DWI will be discussed in this presentation.

MRE and DWI are useful techniques for evaluation of liver fibrosis. Both techniques evaluate physical properties of tissue. MRE measures stiffness of tissue which is dependent on tissue content and organization of tissue components. DWI gives a measure of movement of water molecules that is dependent on temperature and presence of barriers for movement of molecules. Fibrosis characterized by increased collagen fiber content in the extracellular matrix of the liver parenchyma which increases liver stiffness and also creates barriers for water movement that may lead to decreased diffusion. Therefore both techniques are suited for evaluation of liver fibrosis by measuring liver stiffness (MRE) and diffusion (DWI)

MRE

MRE is probably the most sensitive non-invasive technique for detection and staging of liver fibrosis (1). MRE can accurately detect significant fibrosis and exclude cirrhosis with high specificity that is desirable for clinical management decisions (2-4). MRE can be easily integrated into clinical MRI scanner (both 1.5T and 3T) and with routine liver imaging protocols. MRE is a breath hold technique that can be performed in 2D or 3D method. The most common technique is the 2D GRE technique that is available in several leading institutions. The software automatically generates stiffness maps for evaluation of liver. The liver stiffness measured with MRE correlates with fibrotic content of the liver biopsy (5). Although presence of inflammation is a known confounding factor for ultrasound based elastographic techniques, studies till date do not show any such influence (4,5,6). However acute inflammation, acute cholestasis, portal hypertension and passive congestion can increase liver stiffness and therefore MRE may not accurately assess liver fibrosis in the presence of these conditions.

An important advantage of MRE is that it is not affected by the presence of hepatic steatosis or high BMI. MRE can differentiate simple steatosis from steatohepatitis (7). Recently several new clinical indications have emerged for MRE of liver. Some of them are a) assessment of liver fibrosis due to methotrexate; b) liver fibrosis secondary to post Fontan status; c) longitudinal clinical follow up of patient; d) assessment of treatment response; e) prediction of portal hypertension and esophageal varices; f) decompensation in patients with advanced fibrosis and cirrhosis. With its established accuracy and emerging clinical applications, MRE has potential to replace liver biopsy as the reference standard for liver fibrosis assessment.

DWI

DWI is a sensitive technique and decrease in liver signal due to diffusion is quantified as apparent diffusion coefficient (ADC). Liver fibrosis leads to reduced ADC values. Studies using different cut-off values have demonstrated that DWI is an accurate technique for detection of fibrosis and cirrhosis (8-12). Few studies however have shown that ADC is not useful to differentiate normal liver from fibrotic liver (13). Comparison between various DWI studies are hampered by different b values used and different methods for ADC calculation. Optimal b values remain unknown. ADC incorporates both diffusion and perfusion. Therefore perfusion remains a major contributor for the ADC values (14, 15) Many use b=0 which has perfusion effects. Intravoxel incoherent motion (IVIM) technique that is promising for separating and measuring the perfusion and pure diffusion effects is promising for accurate quantification of liver fibrosis (14-15). DWI however is promising for detection of advanced fibrosis and cirrhosis and its differentiation from normal liver (16).

MRE vs. DWI.

Both MRE and DWI have similarities of : quick, fast sequence; easily incorporated to existing protocols; non contrast technique; both evaluate physical property; both assume isotropic structure of liver parenchyma; affected by perfusion/portal hypertension and both may be influenced by presence of inflammation. However MRE is not affected by presence of hepatic steatosis whereas DWI may be affected as fat suppression techniques are used in DWI. Current evidence shows that MRE is more

reliable in staging liver fibrosis as compared to DWI with high sensitivity, specificity and overall accuracy (17).

Summary

MRE and DWI are useful non invasive techniques for evaluation of liver fibrosis. Both techniques have advantages and limitations. Currently, MRE is more accurate technique than DWI for evaluation of liver fibrosis.

References

1Venkatesh SK, et al. J Magn Reson Imaging 2013;37(3):544-55
2Yin M, et al. Clin gastroenterol hepatol 2007; 10L1207-1213
3Huwart L, et al. Gastroenterology 2008; 135(1):32-40
4Venkatesh SK, et al. Eur Radiol 2014;24(1):70-8
5Venkatesh SK, et al. Magn Reson Med 2013 (epub ahead of print)
6Asrani S e tl al J Hepatol 2013 (epub ahead of print)
7Chen J, et al. Radiology 2011; 259(3):749-56
8Taouli B e t al. Am J Roentgenol 2007;1889(4):799-806
9Koinuma et al. J Magn Rson Imaging 2005; 22(1):80-85
10Lewin et al. Hepatology 2007;46(3):658-65
11Girometti et al. J Magn Reson Imaging 2008; 28(2):411-19
12Taouli B et al. J Magn Reson Imaging 2008; 28(1) 89-95
13Sandrasegaran K, et al. Am J Roentgenol 2009; 13(6):1556-60
14Patel et al. J Magn Reson Imaging; 2010;31(3):589-600.
15Luciani et al, Radiology 2008; 249(3):891-99
16Chandarana H et al. Eur J Radiol 2010; 76:348-58
17Wang QB et al. Hepatology 2012;56:239-47.