MRE in Clinical Practice: Evaluating Liver Fibrosis without Biopsy

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Introduction

The management of chronic hepatitis B and C involves identifying patients at risk of disease progression as not all patients develop complications of liver disease. Guidelines on patient selection for therapy rely on the presence of liver inflammation and fibrosis. Liver inflammation can be evaluated through the use of serum tests. The gold standard for diagnosis of liver fibrosis is liver biopsy. Liver biopsy has potential complications and consequently patients are often anxious and prefer to avoid this invasive procedure. Chronic hepatitis is treated with antiviral therapy. Many patients with minimal or no fibrosis defer therapy due to the high expense and known side effects of antiviral treatment, but opt for therapy if they have advanced fibrosis. Some patients may also want to know their degree of fibrosis as a general indicator of prognosis. In these cases, the confirmation and accurate staging of disease is necessary.

The traditional gold standard to diagnose and stage chronic liver disease is liver biopsy and consensus groups recommend the routine performance of liver biopsy prior to the initiation of antiviral therapy for chronic hepatitis. However, the study by Andriulli et al of 535 patients with viral hepatitis showed that knowledge of the grade and stage of chronic hepatitis were considered of value by the treating physician in only approximately 60% of cases, and antiviral treatment was not changed in 81% of patients. In another study, Saadeh et al show that while biopsy provided useful information regarding staging, prognosis, and treatment decisions, the biopsy did not yield new diagnoses in patients with chronic hepatitis.

Liver biopsy is associated with pain in 30%, severe complications in three per 1,000, and death in three per 10,000 patients. In addition, sampling variability is one of the major limitations of liver biopsy. Recent studies suggest that biopsy is approximately 80% accurate in staging liver fibrosis and may even miss advanced fibrosis of cirrhosis in 30% of patients. This implies that patients with chronic hepatitis who are candidates for antiviral therapy face a decision to undergo a procedure for which there is much apprehension, a finite complication rate, personal and societal costs, and the potential for inaccurate information on disease staging or a missed diagnosis.

A new option for evaluating liver fibrosis is MR Elastography (MRE). MRE non-invasively measures liver stiffness by employing low frequency sound waves in combination with MRI to generate "elastograms." Elastograms are maps of tissue stiffness shown on a color scale ranging from soft to hard.

The following study describes the initial experience of non-invasive evaluation of liver fibrosis with MRE in patients who refused or had contraindications for liver biopsy.

Clinical Study

Thirty-eight patients with chronic hepatitis B (HBV) who refused or had contraindications to liver biopsy underwent an MRE of the liver. Liver fibrosis was suspected in 85% of patients; 15% were receiving treatment and referred from other centers for confirmation of liver fibrosis. The patients’ mean age was 57 years. Liver function tests were abnormal in 25% and normal in 75% of patients. Due to perceived unacceptable risk, 90% of the patients refused liver biopsy, while liver biopsy was contraindicated in 10%.
Method
MRE was performed at the end of a routine MRI liver study on a 1.5T MR scanner (GE Healthcare, HDx 15.0). The MRE exam involves a liver MRE sequence with four axial sections of 10mm thickness through the largest axial cross section of the liver. Mean stiffness was calculated by placing a region of interest (ROI) on automatically generated stiffness maps excluding liver edges and major vessels.

Results
MRE was successful in all but one patient who had high liver iron content. One experienced radiologist performed the evaluation of the stiffness maps. Literature reports were used as guidance for differentiating elevated liver stiffness representative of significant fibrosis. Using MRE, 55% of the patients had liver stiffness indicating fibrosis and 42% of the patients had normal liver stiffness.

Management
Liver stiffness from MRE and serum viral DNA levels were considered for management decisions. Among the patients suspected of liver fibrosis, 45% had normal liver stiffness and low serum viral DNA levels and did not receive treatment. Another 16% of patients with mildly elevated liver stiffness and low viral DNA serum levels also received no antiviral therapy and were followed up with regular serum viral DNA and liver function tests. The remaining 38% of patients with elevated liver stiffness and high viral DNA levels received antiviral treatment. Among the six patients who were on antiviral therapy, MRE confirmed fibrosis in four patients and treatment was continued. In two patients with normal liver stiffness, antiviral therapy was stopped in one patient with no detectable serum viral DNA levels while treatment was continued in the other patient with high serum viral DNA levels.

The patients are currently undergoing clinical follow up.

Case One
A 67-year-old male with 30-year history of chronic hepatitis B had HBV load <1000 copies/mL. Liver function tests were normal. The patient refused percutaneous liver biopsy.

MRE Finding
The mean stiffness of the liver was consistent with the absence of fibrosis. The patient is now on regular follow-up.
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About the facility
The National University Hospital (NUH), a member of the National University Health System (NUHS), is a tertiary specialist hospital that provides advanced, leading-edge medical care and services. Equipped with state-of-the-art facilities as well as dedicated and well-trained staff, the NUH is a major referral center that delivers tertiary care for a wide range of medical and dental specialties including Cardiology, Gastroenterology & Hepatology, Obstetrics & Gynecology, Oncology, Ophthalmology, Pediatrics and Orthopedic Surgery. It is the principal teaching hospital of the NUS Yong Loo Lin School of Medicine.


Case Two

A 67-year-old female with chronic hepatitis B presented with high HBV viral load. The patient was allergic to local anesthesia (lignocaine).

MRE Finding

The mean stiffness for the ROI was consistent with that of fibrosis. Antiviral therapy was started without confirmation by liver biopsy.

Case Three

A 58-year-old male with chronic hepatitis B and high HBV load refused liver biopsy.

MRE Finding

The mean stiffness of the liver was consistent with that of severe cirrhosis. Antiviral treatment was started one week after MRE.

Summary

For initiation of antiviral treatment, liver stiffness with MRE and viral DNA load influenced clinical decision for antiviral treatment. For patients on antiviral treatment, elevated liver stiffness was interpreted as fibrosis present and antiviral treatment was continued. Liver function tests did not influence decision in the majority of patients.

Liver MRE provides clinicians useful information for detection of liver fibrosis or confirmation of cirrhosis in the management of patients with chronic liver disease.