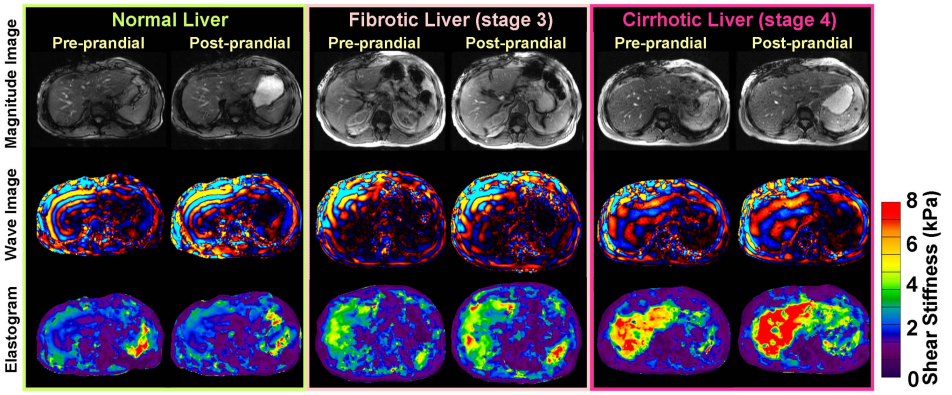
MR Elastography of Dynamic Postprandial Hepatic Stiffness Augmentation in Chronic Liver Disease

M. Yin[1], J. A. Talwalkar[2], S. K. Venkatesh[3], and R. L. Ehman[1]

[1]Department of Radiology, Mayo Clinic, Rochester, MN, United States, [2]Division of Gastroenterology & Hepatology, Mayo Clinic, Rochester, MN, United States, [3]Diagnostic Radiology, National University of Singapore, Singapore

Introduction: Mesenteric blood flow increases markedly in response to the presence of food in the gut, with portal blood flow increasing up to 100% or more postprandially, compared with the fasting state (1). If the impedance to portal outflow remained constant, the increased flow would result in an increase in portal venous pressure. Yet, in normal humans, the portal venous pressure remains stable after eating, due to a reflex decrease in hepatic sinusoidal resistance (1). In contrast, patients with cirrhosis typically experience a 30-40% increase in hepatic venous pressure gradient (HVPG) after eating (2-3). It is thought that mechanical distortion of the intrahepatic vasculature caused by fibrosis impairs the autoregulatory mechanism (4). The repeated episodes of transient portal hypertension after eating are thought to accelerate the development of portal-systemic varices (3). Increased portal pressure may cause stretching of hepatic parenchyma and there is now evidence that stretching of hepatic stellate cells is instrumental in the progression of hepatic fibrosis (5). MR Elastography (MRE) is an MRI-based technique for quantitatively assessing the mechanical properties of soft tissues by visualization propagating shear waves (6). Multiple studies have shown that MRE can demonstrate increased liver tissue stiffness in patients with hepatic fibrosis and that the stiffness increases systematically with the stage of fibrosis (7-8). The *goal* of this research was to measure hepatic stiffness in volunteers and in patients with hepatic fibrosis before and after a test meal which is known to increase mesenteric blood flow. We *hypothesized* that hepatic stiffness would increase postprandially in patients with hepatic fibrosis, presumably due transiently increased portal pressure, whereas this response would not be observed in normal volunteers. If the hypothesis is confirmed, it would provide preliminary evidence that hepatic stiffness reflects portal venous pressure in addition to the presence of fibrosis and the comparison of pre- and postprandial liver stiffness would provide a new potentially useful parameter for characterizing hepatic fibrosis.

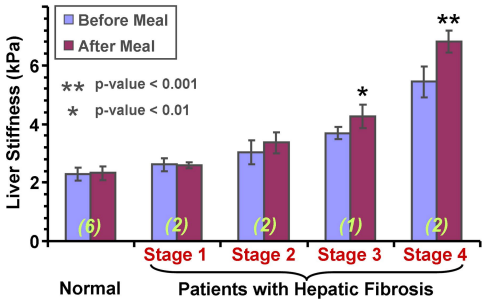
Fig.1



Methods: All experiments were implemented on a 1.5 T whole-body GE imager (Signa, GE Healthcare, Milwaukee, WI, USA). We have previously compiled pre and postprandial hepatic stiffness measurements in 3 normal subjects. At the time that this abstract was written, 3 additional normal volunteers and 7 patients with biopsy-proven hepatic fibrosis were evaluated with MRE (further accrual is ongoing). An initial MRE examination was performed during standardized conditions in the morning after overnight fasting. The imaging procedure lasted 10~15 minutes. Immediately thereafter the subject consumed 470 ml liquid test meal (Ensure plus, 1.5 kcal/ml, Ross products division, Abbott laboratories, Columbus, Ohio) that consists of protein, carbohydrates, fat, vitamins and minerals, with an energy content of 700 kcal. Thirty minutes after finishing this meal, a second identical examination was performed. The imaging protocol included wave image acquisition with a gradient echo based MRE sequence with gradient moment nulling in two selected axial planes with identical imaging parameters as shown in reference (8). Total imaging time for the MRE acquisitions was 64 seconds. Identical parameters, positioning, analysis ROI's were used for both the pre- and postprandial acquisitions.

Results: Fig.1 illustrates fasting and postprandial MRE results in a normal subject, a patient with stage 3 fibrosis, and a patient with cirrhosis. The results in 6 normal subjects, demonstrated no significant change in postprandial hepatic stiffness compared with the fasting state. The results obtained in 7 patients accrued to date have demonstrated a statistically significant increase in hepatic stiffness postprandially in patients with stage 3 and 4 fibrosis, as shown in Fig.2 (the number of subjects in each category is illustrated at the bottom of the corresponding bars)

Fig.2 Pre and Postprandial Liver Stiffness in Patients



Discussion: The results provide preliminary support for the hypothesis that liver stiffness increases following a test meal in patients with advanced hepatic fibrosis, whereas fasting and postprandial liver stiffness are similar in the normal state. This finding suggests the elevated hepatic stiffness identified in patients with chronic liver disease is due to a combination of fibrosis and a functional component that reflects portal pressure – possibly increased tissue tension. Alternatively, the observed dynamic component of liver stiffness may represent a transient change in the mechanical state of cells with contractile characteristics, such as vascular smooth muscle cells and activated stellate cells in the perisinusoidal spaces. The meal induced liver stiffness change can be a predictor of intrahepatic pressure or portal pressure changes. As we know postprandial increase in blood flow in normal subjects usually does not lead to a significant rise in intrahepatic pressure because of autoregulation of portal pressure by the liver. However, in the case of cirrhotic liver, this protective mechanism is not effective and leads to significant rise in portal pressure. This increase in portal pressure leads to increased intrahepatic pressure, which may contribute to increased postprandial liver stiffness. In our previous study, liver patients without fibrosis (stage 0) may have high liver stiffness value due to inflammation (8). However, current study cohort does not contain enough cases for evaluating this situation. We speculate to collect 20 more patients by the time this work to be presented. Considering the spleen stiffness can be affected by portal pressure as well, further investigations on meal induced spleen stiffness changes will be performed as well. It will be worthwhile to separate patients into different groups according to their diagnostic information.

Conclusion: The results provide evidence that MRE-assessed hepatic stiffness in patients with chronic liver disease has a dynamic component that can increase following a test meal. We speculate that this reflects the transient increase in portal pressure that is known to occur in some of these patients postprandially. If confirmed, these findings will provide motivation for further studies to determine the potential value of assessing postprandial hepatic stiffness augmentation for predicting progression of fibrotic disease and the development of portal varices. The technique may also provide new insights into the natural history and pathophysiology of chronic liver disease.

References:

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