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Dynamic Postprandial Hepatic Stiffness Augmentation Assessed With MR Elastography in Patients With Chronic Liver Disease

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Abstract

Objective—MR elastography (MRE) is an MRI-based technique for quantitatively assessing tissue stiffness by studying shear wave propagation through tissue. The goal of this study was to test the hypothesis that hepatic MRE performed before and after a meal will result in a postprandial increase in hepatic stiffness among patients with hepatic fibrosis because of transiently increased portal pressure.

Subjects and Methods—Twenty healthy volunteers and 25 patients with biopsy-proven hepatic fibrosis were evaluated. Preprandial MRE measurements were performed after overnight fasting. A liquid test meal was administered, and 30 minutes later a postprandial MRE acquisition was performed. Identical imaging parameters and analysis regions of interest were used for pre- and postprandial acquisitions.

Results—The results in the 20 subjects without liver disease showed a mean stiffness change of 0.16 ± 0.20 kPa (range, -0.12 to 0.78 kPa) or $8.08\% \pm 10.33\%$ (range, -5.36% to 41.7%). The hepatic stiffness obtained in the 25 patients with hepatic fibrosis showed a statistically significant increase in postprandial liver stiffness, with mean augmentation of 0.89 ± 0.96 kPa (range, 0.17 – 4.15 kPa) or $21.24 \pm 14.98\%$ (range, 7.69% – 63.3%).

Conclusion—MRE-assessed hepatic stiffness elevation in patients with chronic liver disease has two major components: a static component reflecting structural change or fibrosis and a dynamic component reflecting portal pressure that can increase after a meal. These findings will provide motivation for further studies to determine the potential value of assessing postprandial hepatic stiffness augmentation for predicting the progression of fibrotic disease and the development of portal hypertension. The technique may also provide new insights into the natural history and pathophysiology of chronic liver disease.

Keywords

hepatic stiffness; MR elastography; perfusion; postprandial augmentation

Chronic liver disease is a major health problem worldwide. Hepatic fibrosis is the pathologic response of the liver to injurious stimuli that can result in the progression of chronic liver disease. Hepatic fibrogenesis involves the accumulation of collagen, proteoglycans, and other macromolecules within the extracellular matrix [1]. Liver biopsy is considered the reference standard to detect and stage the extent of hepatic fibrosis. However, this procedure

is an invasive method with many limitations, including potentially life-threatening complications, inter- and intraobserver variability with histologic interpretation, and sampling error due to limited specimen sizes [2].

Conventional cross-sectional imaging techniques have limited capability to diagnose liver fibrosis. In clinical practice, imaging studies are usually reserved for the evaluation of suspected or known portal hypertension and hepatocellular carcinoma in cases that have progressed to cirrhosis. In contrast, a number of imaging-based methods, including sonography-based transient elastography [3], CT-based texture analysis [4], and diverse MRI-based techniques [5], have been proposed for the noninvasive diagnosis and staging of hepatic fibrosis for screening or monitoring patients over time.

MR elastography (MRE) [6] is a promising technique for quantitatively assessing hepatic fibrosis via tissue stiffness measurements obtained by studying the propagation of shear waves in the liver. Recent investigations have identified MRE as an accurate, noninvasive imaging technique for detecting occult hepatic fibrosis in patients with chronic liver disease [7–9]. Numerous studies have shown a systematic association between liver stiffness and histologic stage of hepatic fibrosis [10]. Liver stiffness measurements assessed with MRE or ultrasound-based transient elastography techniques have been increasingly used for noninvasive screening, follow-up testing, and guiding treatment in patients with chronic liver disease. However, transient elastography is affected by several factors including body habitus (e.g., obesity, ascites, and narrow intercostal spaces), limited measurement areas, and operator dependence [11]. In contrast, MRE has many advantages that can overcome these limitations [9, 12], although there can be difficulty in subjects with excessive iron load in the liver [13]. Although advanced fibrosis and cirrhosis can be accurately detected with MRE at high sensitivity and specificity, the ability of MRE to discriminate between early stages of fibrosis remains questionable because of several pathologic conditions that can also influence liver stiffness, including hepatic inflammation [14]. Additional studies have elucidated relationships between the measurement of liver stiffness and several factors, including sex, body mass index, and metabolic syndrome [15]; degree of hepatic steatosis [8]; inflammatory grade [14]; and presence or absence of portal hypertension [16].

Dynamic fluctuations in portal pressure after meal ingestion have previously been recognized [17, 18]. Recently, an emerging role for liver stiffness measurements to assess postprandial effects on the liver has been described [19, 20]. Our hypothesis is that MRE-assessed hepatic stiffness may have two components: a static component reflecting intrinsic structural properties, such as changes in the extracellular matrix due to hepatic fibrosis [7–9], and a dynamic component reflecting extrinsic perfusion changes that may lead to transient changes in the mechanical state of cells with contractile characteristics [21]. We hypothesized that hepatic stiffness would increase postprandially in patients with hepatic fibrosis, presumably due to transiently increased portal pressure, whereas this response would not be observed in healthy volunteers. On the basis of our hypothesis, we expected to observe that the mean liver stiffness measured by MRE would be similar in the postprandial state to fasting measurements in healthy volunteers with no known liver diseases, the mean liver stiffness would be increased in the postprandial state compared with fasting measurements in patients with chronic liver disease, and the difference in mean liver stiffness between the postprandial and fasting states would be significantly higher in patients with cirrhosis than in patients with mild to moderate degrees of hepatic fibrosis. If the hypothesis is confirmed, it would provide preliminary evidence that hepatic stiffness also reflects portal venous pressure in addition to the presence of fibrosis, and the comparison of pre- and postprandial liver stiffness could provide a new potentially useful parameter for characterizing hepatic fibrosis.

Subjects and Methods

Volunteer and Patient Recruitment

A total of 20 healthy volunteers and 25 patients with chronic liver diseases were evaluated. This study was approved by our institutional review board. All subjects gave written informed consent after the nature of the study had been explained to them, which included a review of each subject's medical records. Volunteers were considered healthy if they had no previously known history of liver disease or abnormal serum liver enzymes according to their current medical records. Patients with chronic liver disease were included if they had a previous liver biopsy within 12 months of study enrollment confirming the stage of the disease. Exclusion criteria for patients included an absolute contraindication to MRI; prior liver biopsy > 12 months from study enrollment; history of hepatic resection; current involvement with hepatocellular carcinoma or cholangiocarcinoma; current or history of complications related to portal hypertension, including esophageal variceal hemorrhage, ascites, hepatic encephalopathy, or spontaneous bacterial peritonitis; and current or prior medical therapy for underlying liver disease. The study was compliant with HIPAA.

Experiment Setup and Data Acquisition

All experiments were performed on a 1.5-T whole-body system (Signa HDx, GE Healthcare) with an 8-channel phased-array torso coil. As illustrated in Figure 1, subjects were imaged in the supine position, with a 19-cm diameter, 1.5-cm-thick acoustic pressure-activated passive driver placed against the right anterior chest wall with its center level with the xiphoid process. The driver generates significant shear wave motion throughout the majority of the liver, depending on the size of the patient and the size and stiffness of the liver. Continuous longitudinal vibrations at 60 Hz, which is a compromise between wave penetration throughout the liver and elastogram resolution and is consistent with other hepatic MRE literature [7–9, 12], were generated by acoustic pressure waves transmitted from an active driver device (located outside the scanner room as indicated on the far left of Figure 1) into the passive driver via a vinyl tube (2.5-cm inside diameter and 8.2-m long). On the basis of more than 1500 cases performed in clinical practice, no adverse effects from the driver placement or vibrations have been reported to date.

To capture the propagation of the shear waves over a full period of motion, images with four different phase offsets between the motion and the imaging sequence were obtained with a gradient-echo-based multislice 2D MRE sequence. The imaging parameters were TR/TE, 50/20; matrix, 256×64 ; 10-mm slice thickness; 4 axial slices; 1 pair of motion-encoding gradients at 60 Hz with 0 and first gradient-moment nulling (motion encoding sensitivity, $10.1 \mu\text{m/radian}$); and parallel imaging accelerating factor, 2. The acquisition time for this four-slice MRE acquisition was 54 seconds, which was broken into four 14-second breath-holds performed at the end of expiration. Identical parameters and positioning of the slices (at the widest axial cross section of the liver [21]) were used for both the pre- and postprandial acquisitions. Both intervertebral disks and intrahepatic vascular structures were used as anatomic landmarks to facilitate acquiring data at the same slice locations in the pre- and postprandial acquisitions. In practice, we observed that the right lobe of the liver maintains its shape and position very well after food intake. Quantitative elastograms were obtained with a 2D multiscale direct inversion [22] algorithm. The quantity calculated is the effective shear stiffness at 60 Hz, equal to density (assumed to be 1 g/cm^3) times the square of the shear wave speed.

The initial MRE examination was performed in the morning after overnight fasting. The imaging procedure lasted 10–15 minutes. Immediately thereafter, over a 5- to 10-minute period, the subject consumed a 470-mL liquid test meal (Ensure Plus, 1.5 kcal/mL, Ross

Products Division, Abbott Laboratories) that consisted of protein, carbohydrates, fat, vitamins, and minerals, with an energy content of 700 kcal. On the basis of previous investigations of postprandial changes in portal hemodynamics [23–26], a 30-minute delay (± 5 minutes) was used to maximize hemodynamic changes after finishing this meal before performing the second identical MRE examination.

Region of Interest Placement

Identical regions of interest (ROIs) were used for the pre- and postprandial liver stiffness calculations. Image registration of the pre- and postprandial data was performed based on the MR magnitude images before the placement of the ROIs. Then, a common ROI was created for each individual slice and defined according to the following criteria: Include only regions of liver tissue with good wave illumination (i.e., planar wave propagation with a clean and smooth wave front). Exclude areas of nonhepatic tissue (e.g., major vessels larger than 6 pixels that would be at least half the size of the processing kernel, most likely to affect the processing, and practically feasible to segment out). Exclude regions with multipath wave interference (i.e., regions with constructive or destructive wave interference that can affect the accuracy of the stiffness calculations, usually at the corners of the liver). Exclude regions with unreliable signal caused by low-magnitude signal-to-noise ratio (SNR) (< 3 , usually in regions with severe susceptibility artifacts) or phase-difference SNR (< 3 , usually in deep regions of soft livers). The magnitude SNR was calculated as the ratio of the mean MR magnitude signal amplitude to the SD of the signal within the processing kernel. The phase-difference SNR was calculated as the ratio of the wave amplitude in the MRE phase images to the phase noise SD in the processing kernel, excluding regions within half a shear wavelength from the liver boundaries to avoid edge effects from the processing. Mean liver stiffness values were calculated over all pixel values defined by the ROIs placed in the four slices for the pre- and postprandial data. All of this processing was performed using custom in-house software.

Statistical Analysis

The postprandial augmentation for each subject was obtained by simply subtracting the preprandial mean liver stiffness from the postprandial stiffness. For control subjects and patients with different fibrosis stages, the mean pre- and postprandial liver stiffness, postprandial augmentations (both in absolute kilopascal and relative percentage values), and the corresponding SDs were calculated. Study subjects were categorized into three groups: healthy, mild to moderate fibrosis (F0, F1, and F2), and severe fibrosis to cirrhosis (F3, F4). Difference analyses were performed using Bland-Altman plots, which were used to illustrate changes of the mean stiffness difference (i.e., mean postprandial augmentation) for each group. The mean liver stiffness augmentations for groups F0–F2 and F3–F4 were then compared with the mean liver stiffness augmentations obtained from the healthy volunteers using a Kruskal-Wallis test. Comparisons of the mean liver stiffness augmentation for patients with fibrosis stages F0–F2 and F3–F4 were performed using a Wilcoxon's Mann-Whitney test. Finally, exploratory ROC analyses were performed for distinguishing patients with chronic liver disease from the healthy subjects using pre- and postprandial liver stiffness and postprandial augmentation. All statistical analyses were performed using JMP 8.0 (Statistical Discovery, SAS Institute).

Results

The 20 healthy volunteers (8 women and 12 men) had a mean age of 43.6 ± 17.3 years (range, 21–70 years). The 25 patients with chronic liver disease (12 women and 13 men) had a mean age of 54.1 ± 8.7 years (range, 33–67 years). The main chronic liver disease causes were nonalcoholic fatty liver disease ($n = 10$) and chronic hepatitis C ($n = 13$). Of the other

two patients, one had acute cholestatic liver injury with uncertain cause, and the other one had been in long-term methotrexate use for rheumatoid arthritis. The mean aspartate aminotransferase and alanine aminotransferase values for the patient population were 56 ± 38 and 60 ± 46 IU/L, respectively. Serum total bilirubin was normal (0.1–1.0 mg/dL) in 20 patients, and the other five patients had values ranging from 1.4 to 3.3 mg/dL.

In this study, we expected that steatosis extent would not affect liver stiffness measurements as shown in a previous study [8]. Figure 2 illustrates four examples of hepatic MRE examinations performed pre- and postprandially in a healthy volunteer and three patients with different fibrosis stages. In 13 of 20 healthy volunteers, as shown in the first example, we did not observe substantial stiffness augmentation (defined as greater than 10% (0.2 kPa) change from the preprandial level). However, the remaining seven healthy volunteers did have a substantial increase in postprandial liver stiffness, with a mean value of 17.8% (0.35 kPa), ranging from 10% (0.21 kPa) to 42% (0.78 kPa). All measurements were still within the normal range [8]. There was no significant correlation between age, sex, body mass index, recent blood pressure measurements, and stiffness augmentation (linear regression, $R^2 < 0.01$ for all cases). Unexpectedly, a 60-year-old female volunteer with no known liver disease showed significant elevation in liver stiffness after meal ingestion from 1.87 to 2.65 kPa (42% increase).

In 22 of the 25 patients with chronic liver disease, a substantial increase of postprandial stiffness compared with the fasting state was found (augmentation > 10%, ranging from 10% to 63%). The remaining three patients, who did not show more than 10% postprandial liver stiffness augmentation, had biopsy-proven fibrosis stages of F0 (2.12 kPa $\rightarrow$ 2.29 kPa, 8.02% augmentation), F2 (3.52 kPa $\rightarrow$ 3.84 kPa, 9.09% augmentation), and F4 (4.72 kPa $\rightarrow$ 5.15 kPa, 9.11% augmentation). As shown in the second example in Figure 2, a 47-year-old patient with stage F0 fibrosis was observed to have an unusually high increase in liver stiffness from 2.03 to 3.12 kPa (a 53% increase above baseline).

Table 1 and Figure 3 summarize the postprandial liver stiffness changes for the control group and each fibrosis group. In the healthy volunteers, the mean liver stiffness augmentation was 0.16 ± 0.20 kPa ($8.1\% \pm 10.3\%$, ranging from -7% to 42%), which was a small but statistically significant increase (paired Student *t* test between pre- and postprandial liver stiffness values in 20 healthy volunteers, $p = 0.002$). The patient groups with F0–F2 and F3–F4 hepatic fibrosis on liver biopsy had statistically significantly increased postprandial augmentations compared with the healthy volunteers, and the F3–F4 group had significantly higher augmentation than the F0–F2 group (F0–F2 vs control, $p < 0.0003$; F3–F4 vs control, $p < 0.0001$; F3–F4 vs F0–F2, $p < 0.001$). Overall, a significant increase in postprandial liver stiffness augmentation of 0.89 ± 0.96 kPa ($21.1\% \pm 14.5\%$, ranging from 8% to 63%) was observed in all patients with hepatic fibrosis when compared with the healthy volunteers ($p < 0.0001$).

Figure 4 shows the pre- and postprandial liver stiffness values for each individual subject at the top and the difference analyses at the bottom. Subjects with elevated preprandial liver stiffness were prone to have an elevated augmentation in postprandial liver stiffness. The mean difference (i.e., mean augmentation) analyses among the specified three groups (control, F0–F2, and F3–F4) provided additional evidence that mean postprandial liver stiffness augmentation increased progressively with increased fibrosis extent. No overlap was found in the 95% CIs between each pair of groups as shown at the bottom of Figure 4.

Receiver operating characteristic (ROC) curve analyses were performed to explore the possible diagnostic abilities of preprandial liver stiffness, postprandial liver stiffness, and stiffness augmentation (Fig. 5). Postprandial liver stiffness gave the best performance in

distinguishing healthy volunteers from patients with chronic liver disease (area under the ROC curve, 0.97).

Discussion

Summary of Results

These preliminary results support our hypothesis that liver stiffness increases markedly after a meal in patients with chronic liver disease. A much smaller although statistically significant difference between pre- and postprandial liver stiffness in subjects without liver disease was also observed. Moreover, the difference in the mean liver stiffness measured postprandially and while fasting was significantly higher in patients with cirrhosis than it was in patients with mild to moderate hepatic fibrosis. The dynamic changes in liver stiffness are expected to help further define the relationship between liver stiffness and splanchnic circulation in patients with chronic liver disease.

Our results are in agreement with the work reported by Mederacke et al. [20] using the transient elastography technique. These authors found significant postprandial liver stiffness augmentation in 22 of 43 patients with chronic liver disease.

General Explanation of the Results (Ohm's Law)

It is well established that 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 [27, 28]. Many previous studies have shown significant postprandial hyperemia in both normal individuals and subjects with cirrhosis [23, 26, 29]. According to Ohm's law, an increase in postprandial portal blood flow would result in an increase in the hepatic venous pressure gradient if the impedance to portal outflow (i.e., hepatic vascular resistance) does not change. Previous investigators have suggested that pressure-dependent autoregulation of blood flow is present within the hepatic vascular bed that tends to maintain a constant portal pressure gradient [23]. The reduction in hepatic vascular resistance is a dynamic variable that can change the mechanical properties of hepatic tissues via portal venous hemodynamics. If the impedance to portal outflow remained constant due to impaired autoregulation, the increased flow would result in an increase in portal venous pressure (and possibly increased tissue tension as well). In fact, patients with cirrhosis typically experience a 30–40% increase in the hepatic venous pressure gradient after eating [29]. However, in human subjects without liver disease, the portal venous pressure remains stable after eating because of a reflex decrease in hepatic sinusoidal resistance. Therefore, our findings suggest 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.

Postprandial Liver MRE Gives More Information and Better Diagnostic Ability

For conventional abdominal MRI, patients are typically requested to be in the fasting state to eliminate possible motion or susceptibility artifacts from gastrointestinal tract peristalsis. For hepatic MRE, patients are also typically imaged in a fasting state to maintain consistency in the liver stiffness measurement technique and for compliance with the conventional imaging protocol. However, this study suggests that performing MRE after food intake could provide additional information on a portal pressure-dependent dynamic component to hepatic stiffness due to increasing blood flow. Exploratory ROC analyses also supports the notion that either postprandial liver stiffness or augmentation values have a better diagnostic ability for distinguishing fibrotic liver from normal liver than the preprandial liver stiffness value. We speculate that quantitative postprandial augmentation may indicate the degree to which splanchnic vasodilatation can occur in patients with chronic liver disease. This exaggerated

postprandial increase in liver stiffness results from either a meal-stimulated increase in splanchnic, and hence portal venous, blood flow or an increase in intrahepatic vascular resistance, and hence portal pressure, or a combination of both these effects. The areas under ROC curves are lower in this study than in previously published results [8]. This might be due to the smaller patient population in this study or the different population profile.

Although the ROC analysis in this study indicates an improved diagnostic potential using postprandial liver stiffness compared with preprandial stiffness and augmentation, performing hepatic MRE in a fasting state should still be the preferred technique because the current results are preliminary with a small number of patients. Therefore, the exploratory statistical analysis may not be sufficient to establish a solid evaluation of the performance of postprandial liver stiffness, including the possibility that doing so may introduce other unidentified confounding factors into the analysis. For example, it is not clear from this analysis what the impact of the type of test meal or the duration after the meal has on the observed augmentation. Furthermore, as indicated in the study by Mederacke et al. [20], it is possible that significant changes in postprandial stiffness in subjects with normal livers could result in their being misdiagnosed as having fibrosis. Also, if stiffness augmentation is desired, the requirement for an additional MRE examination, a meal, and a delay between the two examinations makes the whole protocol less practical than a single preprandial MRE examination.

Specific situation 1: greater than 10% postprandial augmentation in healthy volunteers—Some of the healthy volunteers in this study (7/20) had postprandial liver stiffness changes greater than 10% (0.2 kPa) after the test meal. These changes did not show significant correlation with either the age, sex, body mass index, or the most recent blood pressure measurements of the subjects. However, even with the increase in stiffness, both the pre- and postprandial liver stiffness measurements remained within the normal range [8]. In these healthy volunteers with no known liver disease, other unidentified factors [30], which were not shown in their documented medical records, may impair the autoregulation mechanism, contributing to increased postprandial liver stiffness.

Specific situation 2: 10% or less postprandial augmentation in patients—Three of the 25 patients had unexpectedly low augmentation (just under 10%) that did not agree with the correlation with fibrosis stage of the other patients. One possible reason could be that postprandial hyperemia simultaneously increased the portal pressure gradient and collateral flow in these patients. Previous investigations have shown that the extent of the collateral circulation determines the portal pressure response to food intake [31]. Patients with extensive collateralization usually show less pronounced postprandial increases in portal pressure because collateral vessels preserve the ability to dilate in response to increased blood flow. Many other studies have shown that the hemodynamic response to a meal in patients with liver cirrhosis is also influenced by the presence and size of esophageal varices and the presence of spontaneous portosystemic shunts [24, 25]. Another possible reason could be postprandial hypotension related to age [32]. Further investigations into such patient-specific confounding factors, such as evaluation of extrahepatic collaterals, are required.

Meaningful Postprandial Liver Stiffness Augmentation

As a promising predictor of intrahepatic pressure or portal pressure changes, the 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. Alternatively, increased portal pressure may cause stretching of hepatic parenchyma, with resulting progression of hepatic fibrosis [33, 34].

Additionally, in the presence of portosystemic shunts, any further increase in portal venous inflow could be diverted directly into the systemic circulation through collateral vessels. The repeated episodes of transient portal hypertension after eating are thought to not only aggravate the metabolic derangement of liver disease but also to increase the risk of variceal rupture [26]. Therefore, a postprandial liver MRE test could be useful to determine optimal pharmacologic or surgical interventions aimed at restoring portal venous flow to the liver by reducing or favoring the occurrence of spontaneous mesenteric-systemic venous shunts. Assuming that the degree of portal venous pressure is an important factor determining the likelihood of bleeding or rebleeding from esophageal varices, the results of the current study would suggest that the evaluation of pharmacologic agents considered for use in the management of portal hypertension should include an assessment of their effects on postprandial liver stiffness augmentation.

Because spleen stiffness can be affected by portal pressure as well [16], it will be worthwhile to perform future investigations on meal-induced spleen stiffness changes. If positive results are obtained, additional longitudinal studies including measurements of hepatic blood flow in this setting would be a logical extension of this investigation.

Conclusions

This preliminary study provides evidence that MRE-assessed hepatic stiffness in patients with chronic liver disease may have a dynamic component that can increase after a meal. We speculate that this reflects the transient increase in portal pressure that is known to typically occur postprandially. These observations 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 be useful for investigations into the natural history and pathophysiology of chronic liver disease. These results also suggest that diagnostic and longitudinal MRE studies should take into account dynamic perfusion effects on hepatic stiffness as a potential cause of variability.

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Fig. 1. Drawing shows experimental setup of hepatic MR elastography. Acoustic pressure waves (at 60 Hz) are generated by active driver, located away from magnetic field of MRI system, and transmitted via flexible plastic tube to passive driver placed over anterior body wall.

Fig. 2.

Examples of pre- and postprandial hepatic MR elastography (MRE) results. This figure shows pre- and postprandial hepatic MRE results in healthy volunteer and three patients with biopsy-proven stage F0, F3, and F4 hepatic fibrosis. As shown in top row, pre- and postprandial elastograms are similar in healthy volunteer. It is obvious that liver stiffness does not change substantially after food intake in this control subject. In three patients with hepatic fibrosis, mean hepatic stiffness is noticeably elevated. For instance, F0 patient has normal liver stiffness (< 2.9 kPa) in fasting state. Thirty minutes after food intake, mean liver stiffness has been elevated to abnormal level of 3.1 kPa. For other two patients with more severe fibrosis, preprandial liver stiffness estimates are already elevated. After meal, postprandial liver stiffness increased by 15% and 48% for patients with F3 and F4 fibrosis, respectively.

Fig. 3.

Chart shows mean postprandial liver stiffness augmentations measured for 20 healthy volunteers and 25 patients with five different biopsy-proven fibrosis stages. Significant differences were found to distinguish three groups of subjects studied (healthy volunteers, patients with F0–F2 fibrosis, and patients with F3–F4 fibrosis). Asterisk indicates $p < 0.001$; double asterisk indicates $p < 0.0001$.

Fig. 4.

Pre- and postprandial liver stiffness measurements and corresponding difference analysis in all subjects.

A, Chart shows liver stiffness data for all healthy volunteers and patients sorted by preprandial liver stiffness values. Mean liver stiffness values estimated before (○) and after (●) test meals are shown with scale along left vertical axis. Connecting needles show corresponding stiffness augmentations, which are enlarged in gray bars with different stiffness scale shown on right vertical axis.

B, Bland-Altman plots for three specified groups: healthy volunteers with no known liver diseases (○); liver patients with mild to moderate fibrosis extent (F0, F1, and F2) (●), and liver patients with severe fibrosis extent (F3, F4) (●). There is no significant difference between pre- and postprandial liver stiffness in healthy volunteers. In patients with liver disease, difference has increased positive shift with higher degrees of fibrosis. Mean difference and corresponding 95% CI for each group are marked with horizontal lines and double-end arrows, respectively, and are listed in table.

Fig. 5.

Exploratory receiver operating characteristic (ROC) analyses assessing diagnostic capabilities of liver stiffness augmentation and pre- and postprandial liver stiffness. ROC analyses show pre- and postprandial liver stiffness data and stiffness augmentation assessing diagnostic capabilities of different quantities for differentiating liver patients with any degree of fibrosis from healthy volunteers with no known liver disease. Both postprandial liver stiffness and augmentation show better prospects for differentiating two groups than preprandial liver stiffness.

TABLE 1
Pre- and Postprandial Liver Stiffness Assessment with MR Elastography

Fibrosis Stage	No. of Subjects	Mean Preprandial Liver Stiffness (kPa)	Mean Postprandial Liver Stiffness (kPa)	Stiffness Augmentation (kPa)	Stiffness Augmentation (%)
Normal	20	2.16 ± 0.24	2.32 ± 0.23	0.16 ± 0.20	8.08 ± 10.33
F0	5	2.64 ± 0.51	3.13 ± 0.50	0.49 ± 0.32	19.66 ± 16.55
F1	4	2.61 ± 0.60	3.09 ± 0.65	0.48 ± 0.15	19.01 ± 7.39
F2	3	2.94 ± 0.52	3.26 ± 0.51	0.32 ± 0.02	11.24 ± 2.17
F3	4	3.78 ± 1.01	4.45 ± 0.98	0.67 ± 0.11	19.25 ± 8.67
F4	8	5.71 ± 1.22	7.38 ± 2.43	1.67 ± 1.37	27.55 ± 19.51

Note—Data are values ± SD.