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Liver stiffness measurements increase after meal ingestion – an important step towards standardization

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Article commented

Arena U, Platon ML, Stasi C, Moscarella C, Asarat A, Bedogni G, et al. Liver stiffness measurement is influenced by a standardized meal in patients with chronic hepatitis C virus at different stages of fibrotic evolution. *Hepatology* 2013; 58: 65-72.

Comment

Transient elastogaphy (Fibroscan) is increasingly used in clinical practice for the non-invasive assessment of liver fibrosis, particularly in patients with chronic hepatitis C (CHC). When the technique was first described 10 years ago, the manufacturing company recommended criteria for reliable results, which included 10 valid measurements with a success rate of at least 60% and an interquartile range between median measurement values of less than 30%. Surprisingly, these criteria were met in only 21/40 transient elastography studies included in a meta-analysis.[1] During the years, it also became apparent that liver stiffness is increased irrespective of fibrosis in a number of conditions, such as cholestasis, non-cirrhotic portal hypertension, liver congestion due to heart failure and necroinflammation. Further studies showing a correlation of liver stiffness with portal hypertension[2] raised the question of potential transient increases in liver stiffness following meal ingestion, and this was indeed confirmed in a preliminary study.[3]

The recent paper by Arena, *et al.* published in *Hepatology* aimed at shedding more light on the effects of meal ingestion on liver stiffness values.[4] The authors included 125 consecutive patients with chronic hepatitis C (CHC) across all stages of fibrosis. All patients had liver stiffness measurements obtained after overnight fasting and 15, 30, 45, 60 and 120 min following a standardized liquid meal of 600 Kcal. Strengths of the study include single disease aetiology, histopathological staging for all patients except those with established cirrhosis, administration of a standardized test meal and measurement of liver stiffness at various time-points post-prandially. Interestingly, liver stiffness significantly increased after the meal, with peak values between 15 and 45 min after ingestion and returned to baseline pre-meal levels within 120 min. Ingestion of a similar to the liquid meal volume of water did not result in increased liver stiffness values. The increase became more pronounced with increasing fibrosis stages and was maximal in cirrhosis, with median stiffness differences ranging from 1.9 KPa in F0F1 fibrosis to 4.7 KPa in cirrhosis. The authors further examined if the post meal delta increase in liver stiffness could enhance the correct classification of fibrosis stage and Child-Pugh class and the diagnosis of presence or absence of esophageal varices; however baseline stiffness values performed better than the delta increase. This was due to increased variability in delta increases in patients with advanced fibrosis and suggests that the adaptation of the hepatic microcirculation to post-prandial hyperemia is variable among individuals.

This study, along with other publications,[3,5,6] implies that the increased liver stiffness in patients with chronic liver disease is due to a combination of liver fibrosis and a functional dynamic component that reflects portal pressure. Interestingly, the increase in liver stiffness after a meal does not correlate with the increase in the portal flow but directly correlates with changes in the hepatic artery blood flow.[5] Therefore, patients showing the expected decrease in hepatic artery blood flow post-prandially (buffering effect) had a significantly lower increase

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in liver stiffness as compared to patients in whom the hepatic artery blood flow increased post-prandially.[5] In the majority of healthy volunteers, liver stiffness as measured with MR elastography does not significantly increase after a meal, suggesting effective compensating mechanisms to counteract the increased blood flow.[6] It would be of interest to determine longitudinally if the delta increase in liver stiffness post-prandially correlates with the chance of decompensation or liver-related death among patients with compensated cirrhosis, therefore if blunted compensating mechanisms are of prognostic significance.

From a practical point of view, this study is an important step towards the standardization of the Fibroscan examination and it strongly suggests that patients should be fasted for at least two hours before liver stiffness is measured. It also implies that a number of false positive results with Fibroscan in previous studies might have been due to meal ingestion prior to the measurements in a number of patients. As Fibroscan is becoming more widely used not only for staging of fibrosis but also for determination of prognosis in patients with advanced fibrosis, it is important to standardize the examination, with implementation of specific quality criteria and determination and validation of disease-specific cutoffs for fibrosis stages. Moreover, as previously suggested, liver stiffness values should be ideally compared with histological quantitative measurements of fibrosis and validated against clinical outcomes.[7,8] Indeed, preliminary results suggest that fibrosis as measured with collagen proportionate area is better related to liver stiffness than histological stage.[9]

In conclusion, liver stiffness increases post-prandially in patients with chronic liver disease, with a peak between 15 and 45 min after meal ingestion, and this increase becomes more pronounced in more severe histological stages. In order to optimize the Fibroscan examination, all measurements should be performed with the patients at least two hours fasted.

CONFLICTING INTERESTS

Nothing to disclose.

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