Elastography: where are we now?

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Liver disease is a significant health problem worldwide, with nonalcoholic fatty liver disease (NAFLD) being the most represented etiology in developed countries and viral hepatitis being more widespread throughout Africa and Asia.

Although differing in etiology, disease progression culminates in liver fibrosis that could progress to liver cirrhosis, and subsequently portal hypertension or hepatocellular carcinoma. Therefore, proper fibrosis staging is needed to diagnose, monitor treatment, and assess the progression of chronic liver disease. Percutaneous liver biopsy is still considered the gold standard for diagnosis and staging liver fibrosis. Liver biopsy is an invasive procedure having potential complications that can be severe in up 1% of the cases, with procedural mortality of 0.01%. Another pitfall is related to sampling error, representing approximately 1/50.000 of the total liver parenchyma. Consequently, its use has been declining over recent years, with researchers trying to find non-invasive serological tests to predict liver fibrosis.[1]

A real breakthrough occurred with the introduction of liver elastography, which has seen unprecedented development in the last ten years since transient elastography (TE) was first introduced in 2003 as a tool to assess liver fibrosis. Currently, manufacturers have developed several elastography methods to assess liver stiffness, which are based on some form of applied stress and the evaluation of the derivate changes in the liver. The possible techniques of delivering stress include a mechanical push with a plunger in vibratory transient elastography or an acoustical push in acoustic radiation force impulse-based US techniques, or continuous mechanical pushes in MR elastography. Each of these techniques has its own advantages and drawbacks. For example, TE is not an imaging technique and therefore is not possible to place with certainty the elastography box in an area of liver parenchyma without liver lesions or free from large vessels. On the contrary, with shear wave elastography (SWE) is possible to obtain a real-time grayscale image to place the region of interest (ROI) in the most desirable area. Also, data show that SWE has a higher inter-operator agreement.[2]

Current guidelines recommend the use of elastography to assess the degree of hepatic fibrosis.[3] However, it is important to remember that all of these methods estimate liver stiffness, which is not a synonym of liver fibrosis, given that several patient-related confounding factors can alter the stiffness values, such as right heart failure (*i.e.* congestion), biliary obstruction, necro-inflammatory activity, digestion state, amyloidosis, alcohol consumption/abstinence or subcapsular or left lobe measurements.[3-5] As a consequence, when one or more of these factors are present, the degree of fibrosis may be overestimated, therefore, a critical reading of liver stiffness measures is required in order to take in account

possible confounding factors. Of notice, while several meta-analyses, have reported a good accuracy for liver fibrosis staging in viral hepatitis, the same cannot be said for NAFLD patients.[6] The current lack of standardized cut-off values could be traced back to two main factors: 1) the heterogeneity of studied populations with limited prevalence of advanced fibrosis; and 2) wide ranges of BMI of enrolled patients in terms of skin-to-liver distance.[6]

Despite the mere fibrosis staging, liver elastography has found its niche role in non-invasive diagnosis of portal hypertension, and since the sixth Baveno Consensus,[7] it has been introduced in clinical guidelines for the non-invasive screening of varices. However, it appears that liver stiffness (LS) can account only for the fixed component of portal hypertension (*i.e.* increase in intrahepatic resistance) and not for the dynamic component (*i.e.* hyperdynamic splanchnic circulation), leaving the stage lights to its left-side companion (*i.e.* spleen elastography) mainly in prediction of esophageal varices.[8-10]

Also, over time it has been demonstrated that liver and spleen stiffness have a pivotal role in risk stratification in patients with advanced compensated liver disease (ACLD). In fact, they have been used in predicting decompensation,[11] development of posthepatic liver failure after liver resection[12] or even the occurrence of HCC[13] and its recurrence after liver resection.[14] More recently, elastography has been proven efficient also in its capability to evaluate treatment response and offer tailored-in risk stratification for complications in patients with advanced chronic liver disease, undergoing treatment with direct antiviral agents.[15]

In conclusion, the existing technology can replace liver biopsy in the majority of patients. All the available techniques have high accuracy for distinguishing patients with no fibrosis or mild fibrosis and patients with cirrhosis. However, it lacks in discriminative ability in intermediate stages that usually shows overlaying in stiffness values. As the technologies progress and manufacturers upgrade machine software, more studies are needed to determine which of the currently available techniques is the most accurate, standardized and reproducible.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—All authors read and approved the final version of the manuscript.