EDITORIAL

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Can Magnetic Resonance Elastography Fill a Niche in the Market for Noninvasive Assessment of Liver Fibrosis?

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See "Magnetic Resonance Elastography and Diffusion Weighted Imaging in the Evaluation of Hepatic Fibrosis in Chronic Hepatitis B" by Tiffany P. Hennedige, et al. on page 401, Vol. 11. No. 3, 2017

Liver fibrosis is a consequence of a wound-healing response to various types of chronic liver injury, and can ultimately lead to liver cirrhosis, portal venous hypertension, and the development of hepatocellular carcinoma, morbidity, and mortality.[1] Thus, it is of paramount importance to assess the presence and degree of liver fibrosis in patients with chronic liver diseases (CLDs) for optimizing surveillance strategy, monitoring disease course, deciding on initiation of therapeutic interventions, monitoring the therapeutic response, and predicting outcomes.[2,3]

Until recently, assessment of liver fibrosis has depended on liver biopsy (LB). However, LB is often limited by its invasiveness and extremely rare, but fatal complications including procedure-related mortality, high cost, low patient acceptance, reluctance of physicians, need for expertise, prolonged procedure time, interobserver/intraobserver interpretational variability, sampling error, and poor reproducibility.[4] Accordingly, various biochemical surrogates for LB, such as the FibroTest, enhanced liver fibrosis test and *Wisteria floribunda* agglutinin-positive human Mac-2 binding protein (M2BP),[5,6] as well as physical surrogates such as transient elastography (TE) and acoustic radiation force impulse elastography, have been proposed to noninvasively assess the fibrotic burden in patients with CLDs.[2] Most recently, advances in magnetic resonance imaging (MRI) have enabled assessment of the degree of liver fibrosis, irrespective of etiology.[7,8]

In this issue of *Gut and Liver*, Hennedige *et al*.[9] compared the accuracy of 1.5-T-based magnetic resonance elastography (MRE) and diffusion-weighted imaging (DWI) (DWI-free breathing [DWI-FB] and DWI-breath hold [DWI-BH]) to assess the degree of liver fibrosis in patients with chronic hepatitis B (CHB). The accuracy for detecting ≥F2/≥F3/F4 stage fibrosis by DWI-FB, DWI-BH and MRE was 0.84/0.76/0.72, 0.72/0.83/0.79 and 0.99/0.99/0.98, respectively. Moreover, the performance of MRE was significantly better than that of DWI-FB and DWI-BH. Although the results of Hennedige *et al*.[9] per se add further evidence regarding the accuracy of MRE in assessing the degree of liver fibrosis and its superiority to DWI, several important issues require attention.

First, the authors excluded patients in whom LB was performed >6 months after MRI assessment, as well as those who received antiviral therapy (AVT) between their LB and MRI assessment, to minimize the influence of potential changes due to the natural disease course or AVT. However, because intervening events, such as changes in viral replication and the corresponding fluctuations of alanine aminotransferase (ALT) level, can occur, the potential bias due to the relatively wide time interval between LB and MRI assessment (6 months) should be considered. The extremely small sample size for each fibrosis stage is another issue. Second, the heterogeneous indications for LB might have confounded the results. If patients received LB for follow-up with or without therapeutic interventions such as AVT, we can hypothesize that the patients were not indicative of AVT or showed appropriate viral suppression with potentially regressed fibrosis due to prolonged AVT. In contrast, if patients underwent LB to decide initiation of AVT, they might have a higher probability of an unstable liver status, such as high necroinflammation with/without intrahepatic cholestasis due to active viral replication requiring the initiation of AVT. All variables above-including prolonged AVT, fibrosis regression, necroinflammation, and intrahepatic cholestasis-can influence

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the diagnostic accuracy of MRE. Indeed, the mean stiffness value of A2 necroinflammation in this study was higher than those of A1 and A2 (5.5 kPa vs 4.3 kPa and 4.1 kPa). Third, detailed clinical information, especially laboratory results, is lacking. Based on this information, the study population should have been selected more carefully to prevent the potential influence of well-known confounders of elastography, such as a high ALT level or heart failure. In addition, the correlation between ALT level and stiffness by MRE should have been investigated. Furthermore, using these clinical variables, the accuracy of MRE could have been compared with those of other simple noninvasive parameters, such as the aspartate-to-platelet ratio index (APRI) or FIB-4, to support the superiority of MRE in assessing the degree of liver fibrosis. Lastly, because LB is an imperfect gold standard, an area under the receiver operating characteristic curve (AUC) value of >0.90–0.95 does not necessarily mean that the predictive accuracy of a given surrogate is approaching diagnostic perfection.[10] In addition, small differences in AUC do not necessarily mean that one noninvasive surrogate has an inferior performance, because whether this difference in the AUC value is due to noninvasive surrogates, LB, or both is unclear. Therefore, the performance of noninvasive surrogates should be evaluated in long-term follow-up, longitudinal studies using solid clinical endpoints, such as the development of hepatic decompensation, hepatocellular carcinoma, or liver-related death.

Despite the aforementioned pitfalls, Hennedige *et al*.[9] conducted a head-to-head comparative study of the diagnostic accuracy of MRE in assessing the degree of liver fibrosis in patients with CHB. Indeed, it has been reported that MRE has the highest accuracy among several other surrogates (AUC>0.90) for assessing fibrotic burden in patients with CLDs.[7] However, few confirmatory studies have been performed compared to other surrogates, such as TE. Although the accuracy of MRE has been confirmed and it has many advantages-such as high specificity for the liver, estimation of the entire liver, being unaffected by obesity, simultaneous assessment of liver and tumor information, simultaneous magnetic resonance spectroscopic evaluation of steatotic burden-the application of MRE for noninvasive assessment of liver fibrosis cannot be expanded until unmet issues, such as the high cost, nonimmediate acquisition of results, needs for specific equipment (mostly available at tertiary academic institutes), low accuracy under conditions of iron overload, nonapplicability to patients with implantable devices, and lack of standardization across platforms, especially for DWI, are resolved.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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