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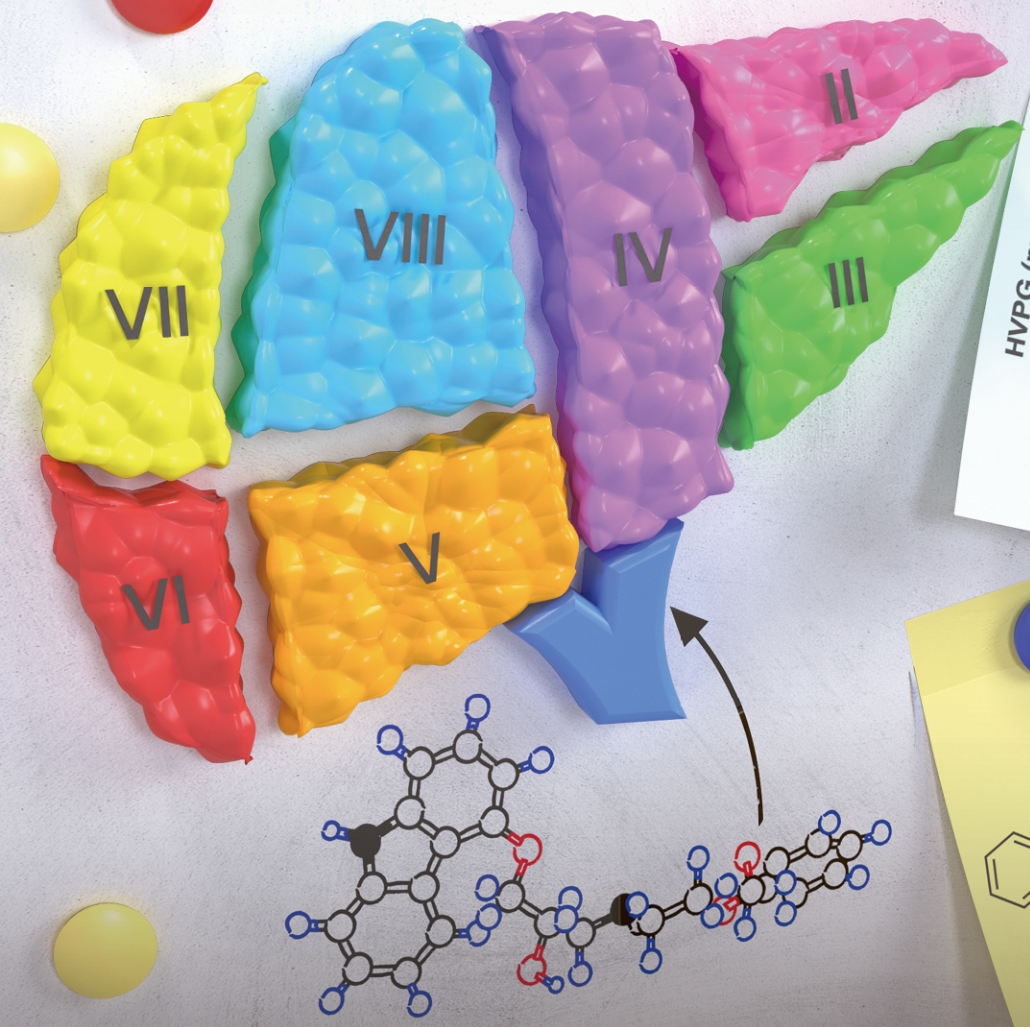

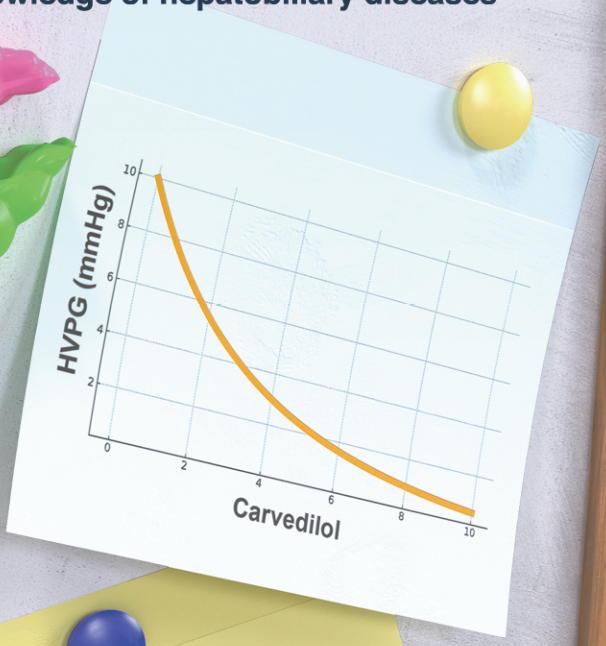

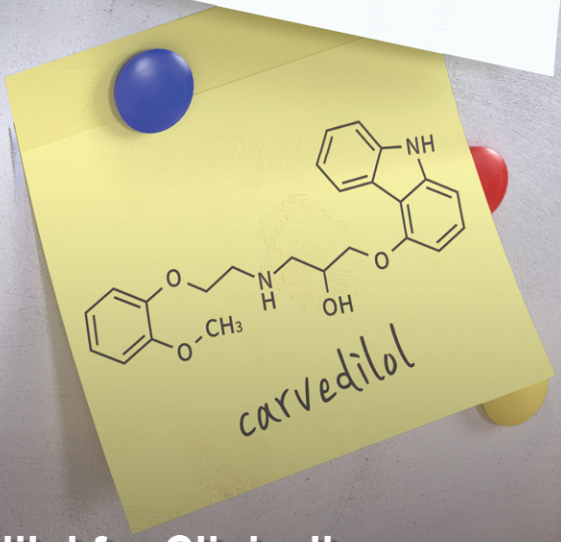

Non-invasive Model guiding Carvedilol for Clinically Significant Portal HTN

Intrapatient variability of tacrolimus on CKD in LT
HCV self-testing and disease burden reduction
MASLD and microbiota
Bariatric surgery for metabolic cirrhosis

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Editorial

Essential tools for assessing advanced fibrosis in metabolic dysfunction-associated steatotic liver disease: Editorial on "Optimal cut-offs of vibration-controlled transient elastography and magnetic resonance elastography in diagnosing advanced liver fibrosis in patients with nonalcoholic fatty liver disease: A systematic review and meta-analysis"

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Keywords: Metabolic dysfunction-associated steatotic liver disease; Fibrosis; Cirrhosis; Noninvasive test

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The global prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is approximately 30%, which contributes to a growing global mortality burden.[1,2] Liver fibrosis is a crucial factor in the prognosis of patients with MASLD. Advanced fibrosis or cirrhosis is an independent factor in the development of hepatocellular carcinoma (HCC) and liver-related mortality in MASLD.[3,4] Therefore, detecting advanced fibrosis is necessary to define high-risk groups for MASLD. The gold standard method for assessing liver fibrosis is histologic finding by liver biopsy.[5] However, liver biopsy is limited in clinical practice because it is invasive and difficult to examine repeatedly.[5] Instead of liver biopsy, noninvasive tests for liver fibrosis have been widely used to assess advanced fibrosis or cirrhosis in patients with MASLD.[6]

In this issue of *Clinical and Molecular Hepatology*, Chon et al. have presented the optimal cut-offs for transient elastography (TE) and magnetic resonance elastography (MRE) in diagnosing advanced liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD).[7] The systematic review and meta-analysis concluded that the cut-off levels of liver stiffness measurement (LSM) for diagnosing advanced liver fibrosis in NAFLD using TE and MRE were 7.1–7.9 kPa and 3.62–3.8 kPa, respectively.[7] The suggested cut-offs performed favorably in terms of diagnostic ac-

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curacy. Recently, the term MASLD was adopted to replace NAFLD.[8,9] In the present study, the authors proposed optimal cut-off levels using TE and MRE in evaluating NAFLD because previous studies were conducted based on NAFLD.[7]

This study had several clinical implications. Various academic societies have recommended clinical care pathways to manage patients with MASLD.[9,10] The key aspect of clinical care pathways in MASLD is the screening and diagnosis of advanced fibrosis. The recommendations indicate that primary care physicians should refer patients with MASLD and advanced fibrosis or cirrhosis to hepatologists.[9,10] Noninvasive tests for assessing advanced fibrosis in MASLD are blood tests (fibrosis-4 [FIB-4] index or NAFLD fibrosis score [NFS]) and imaging tests (TE and MRE).[6,11] While the FIB-4 index and NFS are cheap and easily applicable, their diagnostic accuracy for advanced fibrosis is not very high.[11] Therefore, these are strong tools for the first step in screening liver fibrosis in MASLD. TE and MRE have favorable diagnostic accuracy for advanced fibrosis in MASLD, although they are not easily used in primary care settings.[6] In the present study, the areas under the receiver operating characteristic curves in TE and MRE for diagnosing advanced fibrosis were 0.87 and 0.89, respectively.[7] Individuals with TE or MRE results above the cut-off values should be referred to hepatologists for precise work-up and further management of liver-related outcomes. Therefore, TE or MRE is used as the second step to clarify advanced liver fibrosis in patients with MASLD. Both TE and MRE have several advantages and limitations. TE is rapid, painless, and easy to perform; however, it is difficult to perform in patients with obesity or ascites. The accuracy of TE for detecting liver fibrosis in obese patients with MASLD is not high. There are several strategies for more precise assessment of liver fibrosis individuals with obesity. First, compared with the M-probe of TE, using the XL-probe can reduce TE failure and facilitate reliable LSM in patients with obesity.[12] Second, serum biomarkers derived directly from the extracellular matrix formation and degradation process in the pathogenesis of fibrogenesis and fibrinolysis can be used to assess liver fibrosis in patients with obesity. For instance, enhanced liver fibrosis, Fibrotest, and Hepascore can be used in patients with obesity with TE failure.[11] Lastly, MRE can be preferentially used to assess liver fibrosis in patients with obesity with MASLD. MRE has a higher diagnostic accuracy than TE for advanced fibrosis or cirrhosis in obese patients with MASLD.[13] MRE is superior to TE in identifying the early stage of liver fibrosis but has higher equipment costs.[6] Therefore, combining LSM using TE and serum biomarkers may be a more cost-effective alternative for evaluating liver fibrosis in MASLD. For instance, combined biomarkers such as the Fibroscan-AST (FAST) score, Agile 3+ score, and Agile 4 score have higher diagnostic accuracy for advanced fibrosis or cirrhosis in MASLD than LSM using TE only.[14,15] Therefore, combining LSM using TE and serum biomarkers is a good strategy for assessing liver fibrosis in MASLD if MRE is unavailable.

TE and MRE play a role in selecting patients for the treatment of metabolic dysfunction-associated steatohepatitis (MASH). Recently, resmetirom, a thyroid hormone receptor-β-selective agonist, was first approved for treating MASH with F2/F3 fibrosis.[16] Resmetirom treatment resulted in MASH resolution and improvement in liver fibrosis by at least one stage compared with placebo.[17] In clinical practice, it is very difficult to perform routine liver biopsy for selecting patients with MASH with significant or advanced fibrosis. Therefore, noninvasive tests can be useful for screening and diagnosing significant or advanced fibrosis in patients with MASH. TE and MRE have been used for selecting patients with MASH with significant or advanced fibrosis in new drug development, including resmetirom.[17,18] TE and MRE are becoming increasingly utilized in real practice and clinical trials for MASH treatment.

As mentioned previously, TE and MRE are essential tools for assessing advanced fibrosis in the clinical care pathway and patient selection for MASH treatment. The suggested cut-off values of TE and MRE for advanced fibrosis in the present study can help manage patients with MASLD or MASH.[7] Therefore, precise methods for diagnosing advanced fibrosis or cirrhosis in patients with MASLD should be developed in the future. Combining imaging studies (TE

Abbreviations:

FAST, Fibroscan-AST; FIB-4, fibrosis-4; HCC, hepatocellular carcinoma; LSM, liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; NFS, NAFLD fibrosis score; TE, transient elastography

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and MRE) with serum biomarkers can be used for screening and confirmation of liver fibrosis in MASLD. For example, the FAST score (TE and AST) and MEFIB index (MRE and FIB-4 index) had diagnostic accuracy for advanced fibrosis or cirrhosis in patients with MASLD.[14,19] Moreover, recent studies have challenged genetic polymorphisms, circulating microRNAs, and proteomics as novel serum biomarkers for advanced fibrosis or cirrhosis in patients with MASLD.[20-22] If novel serum biomarkers show favorable diagnostic accuracy for advanced fibrosis in MASLD, combining imaging studies and novel serum biomarkers may be a more promising method for stratifying disease severity.

Author's contribution

W Sohn contributed to the conception of the work, drafted the manuscript, and contributed to critical revision.

Conflicts of Interest

The author has no conflicts to disclose.

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