Prediction of Minimal Hepatic Encephalopathy

By definition, minimal hepatic encephalopathy (MHE) suggests the presence of cognitive defects in patients with liver disease or portal-systemic shunting in the absence of both overt hepatic encephalopathy (OHE) and other known causes of these defects. These cognitive deficits are difficult to find by routine physical or neurological examinations and require specific neuropsychological or neurophysiological testing.[1] MHE is defined as an ambiguous cognitive deficit entailing psychomotor slowing and loss of attention. Visual perception and fine motor performance are also impaired, whereas verbal ability tends to be preserved. MHE can reduce the patient's quality of life. Consequently, it is important to develop ways to predict MHE.

Liver fibrosis occurs in response to almost all causes of chronic liver insults, and the initiation of its deposition imposes an important phase in chronic liver disease. Eventually, without appropriate interventions, liver fibrosis progresses leading to changes in liver morphology, deterioration of liver function and hemodynamics, complications due to portal hypertension, and an increased inclination for hepatocarcinogenesis. Because the complications of liver cirrhosis usually develop in patients at an advanced stage, the early detection of advanced liver fibrosis and cirrhosis and the evaluation of their severity are important for increasing the effectiveness of treatment. Currently, liver biopsy is the gold standard for evaluating liver fibrosis. However, this procedure is very invasive, and clinicians should consider the sampling error and interpretational variability involved.[2,3] The hepatic venous pressure gradient (HVPG) is also a standard tool for the diagnosis and treatment of liver cirrhosis and suspected portal hypertension.[4] It is useful for evaluating patients and performing therapeutic interventions, and it is an important prognostic factor. Because repeated liver biopsy or HVPG is not performed routinely to provide information on the clinical progression of cirrhosis, noninvasive methods are required to replace these invasive procedures, such as

serum biomarkers[5] or the measurement of liver stiffness with transient elastography (TE).[6] A significant correlation between TE values and HVPG was demonstrated by Vizzutti *et al*. suggesting that TE may reflect a progressive rise in portal pressure mainly due to increased hepatic vascular resistance caused by fibrillar extracellular matrix accumulation.[7]

Recently, several studies have suggested that liver stiffness is associated with liver-related complications. TE has been introduced for evaluating liver fibrosis with reliable results and for assessing the risk of developing liver-related complications and hepatocellular carcinoma.[8,9] Some reports have suggested that TE can predict the prognosis of liver cirrhosis.[10,11] Other reports support the use of these measures in patients with alcoholic liver disease[12] and liver transplantation.[13]

Cognitive impairment is one of the main characteristics of MHE, although a number of patients with cognitive problems do not show neuropsychological or neurophysiological abnormalities.[14] Currently, the psychometric hepatic encephalopathy score (PHES) is recommended as a tool for diagnosing MHE. It involves five paper-and-pencil tests: the digit symbol test, number connection test A, number connection test B, serial dotting test, and line tracing test. Methods for evaluating MHE were introduced in this article; however, these evaluations were not objective, but reflected the clinician's subjective opinion. A standard and simple test for the detection of MHE is needed. In the current issue of the *Saudi Journal of Gastroenterology*, attempts have been made to predict MHE in cirrhosis using liver stiffness and HVPG.[15] In this report, TE and HVPG were correlated with the Child's and Model for End-Stage Liver Disease (MELD) scores, whereas TE and HVPG were insufficient for predicting MHE in patients with cirrhosis. This study is meaningful in that it represents the first attempt to assess whether TE and HVPG can predict the occurrence of MHE in patients with cirrhosis, even though they did not result in the significant difference to predict MHE in the present study. From a clinical point of view, clinicians are interested in several aspects of the course of cirrhosis. Does the extent of liver fibrosis influence the prognosis? How long does it take for decompensated cirrhosis or hepatocellular carcinoma to develop in patients with cirrhosis? Is it possible to predict the occurrence of complication? If it is, how much is it helpful? We need simple, objective, and reproducible methods that can assess cognitive impairment in patients with cirrhosis.

If the clinician can evaluate the possibility of MHE digitally, it is helpful to take care of cirrhotic patients. TE and HVPG are the reliable instruments to show the state of patients in digital, even though they cannot predict MHE in patients with cirrhosis in the present study. Especially, TE is currently accepted as a promising noninvasive method for liver fibrosis worldwide and can provide useful information on the clinical progression to cirrhosis, hepatocellular carcinoma, and liver-related mortality. Large, well-conducted trials are needed to evaluate the definite potential of TE for predicting liver-related complications including MHE.

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