Non-invasive algorithm for detecting advanced liver fibrosis in chronic hepatitis B patients

HLY Chan *, VWS Wong, GLH Wong, PCL Choi

KEY MESSAGES

1. Liver stiffness measurement (LSM) using FibroScan is superior to serum test formula to diagnose advanced liver fibrosis.

2. Combination of LSM and the Forns index (LSM-Forns algorithm) can improve the accuracy of LSM to predict advanced liver fibrosis.

[1] HLY Chan, [1] VWS Wong, [1] GLH Wong, [2] PCL Choi

The Chinese University of Hong Kong:
[1] *Department of Medicine and Therapeutics*
[2] *Department of Anatomical and Cellular Pathology*

* Principal applicant and corresponding author: hlychan@cuhk.edu.hk

Chronic hepatitis B is the most important cause of liver cirrhosis in Asia. Liver fibrosis is the intermediate stage to liver cirrhosis. Determining severity of liver fibrosis is important to determine the prognosis, risk of hepatocellular carcinoma, and need for antiviral therapy. Liver biopsy is the gold standard, but it is limited by its invasiveness and risk of bleeding. Transient elastography by the Fibroscan is a non-invasive measure for severity of liver fibrosis. Liver stiffness is measured based on shear wave velocity across the liver. It is accurate to determine advanced fibrosis in chronic hepatitis B and C patients, but the accuracy for mild-to-moderate fibrosis is less optimal.[1] Various serum indices are developed to measure liver fibrosis in viral hepatitis, including aspartate aminotransferase–to-platelet ratio-index, Forns index, FIB-4, Hui index, and Fibroindex. We investigated a combined algorithm of a serum test formula with Fibroscan for the evaluation of severity of liver fibrosis in chronic hepatitis B patients. A biopsy cohort of 156 hepatitis B patients was used as the training cohort,[2] and the resultant algorithm was validated in an independent cohort of 82 patients with liver biopsy.

Liver stiffness measurement by Fibroscan was superior to that by all other serum test formulae, consistent in both the training and the validation cohorts.[3] The area under the receiver operating characteristics curve (AUROC) for Fibroscan was 0.88 (95% confidence interval [CI], 0.85-0.91, P<0.001) in the training cohort and 0.80 (95% CI, 0.68-0.92, P<0.001) in the validation cohort. Among various serum tests formulae, Forns index was best in diagnosing advanced fibrosis, with an AUROC of 0.70 (95% CI, 0.62-0.78, P<0.001) in the training cohort and 0.72 (95% CI, 0.60-0.85, P<0.001) in the validation cohort.

By combining the liver stiffness measurement and Forns index, an algorithm superior to either test was derived. A low liver stiffness or a Forns index of <5.2 could exclude >60% patients with mild fibrosis and avoided the need of liver biopsy. A high liver stiffness together with a Forns index of >8.4 could confirm advanced liver fibrosis with <1% error. This non-invasive algorithm can be conveniently used in the primary care setting, as Forns index only requires common blood tests measuring levels of platelet, gamma-glutamyl transpeptidase, and cholesterol. For patients excluded for advanced liver fibrosis, only observation is needed. For patients with uncertain liver fibrosis, they should be referred to specialist for consideration of liver biopsy. Those confirmed to have advanced liver fibrosis by the combined algorithm can proceed directly to antiviral therapy without the need of an invasive liver biopsy. With this algorithm, liver biopsy can be avoided in approximately 50% of patients.

Acknowledgements

References

1. Wong VW, Chan HL. Transient elastography. J Gastroenterol Hepatol 2010;25:1726-31.
2. Chan HL, Wong GL, Choi PC, et al. Alanine aminotransferase-based algorithms of liver stiffness measurement by transient elastography (Fibroscan) for liver fibrosis in chronic hepatitis B. J Viral Hepat 2008;16:36-44.
3. Wong GL, Wong VW, Choi PC, Chan AW, Chan HL. Development of a non-invasive algorithm with transient elastography (Fibroscan) and serum test formula for advanced liver fibrosis in chronic hepatitis B. Aliment Pharmacol Ther 2010;31:1095-103.