GFM Gastroenterology and Functional Medicine

ORIGINAL ARTICLE

Liver status and metabolic-dysfunction associated steatotic liver disease/steatohepatitis presence by Fibroscan® in patients with chronic hepatitis B: A Faraday study

Mustafa Kemal Celen[1], Cigdem Mermutluoglu[1], Fethiye Akgul[2], Pinar Cakmak[3], Tuba Damar Cakirca[4], Ismail Yildiz[5], Yesim Tasova[6], Yasar Bayindir[7,*]

[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Dicle University, Diyarbakir 21830, Turkey
[2]Department of Infectious Diseases and Clinical Microbiology Batman Training and Research Hospital, Batman 72000, Turkey
[3]Department of Infectious Diseases and Clinical Microbiology, Mardin Training and Research Hospital, Mardin 47100, Turkey
[4]Department of Infectious Diseases and Clinical Microbiology, Sanliurfa Training and Research Hospital, Sanliurfa 63200, Turkey
[5]Department of Biostatistics, Faculty of Medicine, Dicle University, Diyarbakir 21830, Turkey
[6]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Cukurova University, Adana 01380, Turkey
[7]Department of Infectious Diseases and Clinical Microbiology Ankara Private Guven Hospital, Ankara 6540, Turkey

ABSTRACT

Background and Objectives: Evaluation of liver fibrosis is imperative in the management of chronic hepatitis B. Metabolic dysfunction-associated steatotic liver disease (MASLD) or metabolic dysfunction-associated steatohepatitis (MASH) with necroinflammation contribute significantly to liver damage. This study aims to investigate the role of vibration-controlled transient elastography (FibroScan®) as a non-invasive method for diagnosis and treatment follow-up. **Methods**: The study was prospectively planned in four different centers. Patients who were positive for hepatitis B surface antigen for more than 6 months and had an HBV-DNA > 2000 IU/mL underwent liver biopsy and FibroScan®. FibroScan® was performed before antiviral therapy and 1 year after treatment. **Results**: A total of 70 patients were included in the study. The mean age was 37.1 years, and 70.0% of the patients were male. The concordance rate with simultaneous elastography in 68 biopsies was 97.1% ($P < 0.001$). In 66 patients (97.0%), the liver fibrosis score was $\geqslant 2$ or the hepatic activity index was $\geqslant 6$. At the beginning of antiviral treatment, 19 patients (27.1%) had MASLD and 6 patients (8.6%) had MASH. The MASLD rate decreased to 25.7% ($P = 0.064$), and there was no change in MASH rate at the end of 1 year. The concordance rate with liver biopsy was found to be acceptable. **Conclusion**: FibroScan® was as useful as liver biopsy in the evaluation of chronic viral hepatitis-associated fibrosis as well as in the diagnosis and follow-up of concomitant MASLD/MASH.

Key words: chronic hepatitis B, metabolic syndrome, hepatic fibrosis, hepatic steatosis, metabolic-dysfunction associated steatotic liver disease/metabolic-dysfunction associated steatohepatitis, FibroScan®

INTRODUCTION

Chronic hepatitis B (CHB) is a significant global public health concern that affects millions of individuals. It increases the risk of severe complications such as liver cirrhosis and hepatocellular carcinoma (HCC).[1–3] There is currently no cure for CHB. Nucleos(t)ide antivirals suppress viral replication and reduce liver inflammation

***Corresponding Author:**
Yasar Bayindir, Department of Infectious Diseases and Clinical Microbiology Ankara Private Guven Hospital, Ankara, 6540, Turkey. E-mail: yasarb44@hotmail.com
Received: 24 February 2025; Revised: 2 March 2025; Accepted: 23 April 2025
https://doi.org/10.54844/gfm.2025.893

and fibrosis. However, fibrosis persists in a certain group of patients with or without therapy. Therefore, it is critical to monitor liver fibrosis to prevent the progression to advanced stages, which leads to severe liver damage.[2]

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly nonalcoholic fatty liver disease, is a clinicopathologic description of patients with little or no history of alcohol consumption who have histological features indicative of liver damage like that induced by alcohol. Features range from fat accumulation in hepatocytes (simple hepatic steatosis) to necroinflammatory (steatohepatitis). Fibrosis may also be seen and is called metabolic dysfunction-associated steatohepatitis (MASH), formerly nonalcoholic steatohepatitis. MASH progresses to cirrhosis in 20% of patients. MASH is now recognized as a leading cause of cryptogenic cirrhosis.[4,5]

It is generally accepted that hepatic steatosis causes or triggers fibrosis in patients with CHB.[6] Obesity, metabolic syndrome, MASLD, and MASH may also accompany comorbidities with CHB.[7–9] There is increasing evidence that hepatic steatosis and metabolic dysfunction increase the risk of progression to HCC in patients with CHB, and patients with chronic liver disease, including CHB, should be evaluated for MASLD.[10]

Liver biopsy is the gold standard to assess steatosis and fibrosis. It is used for both diagnosis evaluation and during treatment in patients with CHB.[2–11] While liver biopsy is a valuable diagnostic tool, it has several disadvantages, including subjectivity, risk of complications, fears and concerns of patients, and invasiveness. There is a significant need for simple, safe, and non-invasive methods of fibrosis evaluation.[12–13] FibroScan® is a non-invasive diagnostic tool and has been validated for the assessment of liver fibrosis in CHB patients. There is a significant correlation with histological fibrosis stages and high diagnostic accuracy.[2,14,15] However, biopsy is mandatory by insurance companies in some countries before starting treatment for CHB.

The aim of the study was to evaluate the consistency between liver biopsy and FibroScan® evaluation of liver stiffness measurement (LSM) for fibrosis and controlled attenuation parameter (CAP) for steatosis in patients with CHB. The secondary aim of the study was to demonstrate the efficacy of FibroScan® for the follow-up of patients with CHB after 12 months of antiviral therapy.

MATERIALS AND METHODS

Study population and data collection

Patients aged 18 years and older who were positive for hepatitis B surface antigen positivity for more than 6 months and had an HBV-DNA level > 2000 IU/mL were included in the study. Written informed consent was obtained from all participants. The exclusion criteria were established as the presence of cirrhosis, alcohol consumption > 140 g/week for females and > 210 g/week for males, and hepatitis C, hepatitis D, and/or HIV coinfections. The baseline characteristics including patient demographics, body mass index, comorbidities, LSM and CAP *via* transient elastography (FibroScan®), liver ultrasound, HBV serology, platelet count, alanine aminotransferase (ALT), and HBV viral load were collected.

Evaluation of liver status and antiviral therapy

All patients underwent liver biopsy and FibroScan® before initiating antiviral therapy. There was a maximum interval of 2 weeks between the liver biopsy and the FibroScan®. Transient elastography was performed by a certified operator, using the M probe for patients with skin to capsule distance < 2.5 cm or an XL probe for patients with skin to capsule distance > 2.5 cm. Patients were fasted for > 2 h before the FibroScan®. At least 10 successful measurements were performed and recorded.[16]

Fibrosis stage by LSM and steatosis by CAP were investigated on FibroScan® for MASLD and MASH. Patients with obesity or diabetes with a CAP value > 240 dB/m were diagnosed with MASLD. Patients with a normal body mass index and patients without diabetes who had at least two risk factors for metabolic dysfunction were also diagnosed with MASLD. Patients with MASLD and concomitant necroinflammation in the liver were diagnosed with MASH. Necroinflammation was defined as LSM $\geqslant$ 7.2 kPa in patients with MASLD or LSM > 5.5 kPa in patients with liver injury (histologic and/or ALT > non-specific uptake).

The study protocol was approved by the Ethics Committee of Dicle University (Protocol number: 2022/261). Our trial was registered to Clinical Trials as a completed trial retrospectively, and the trial registration ID is NCT06573190.

Statistical analysis

The SPSS 21.0 statistical software for Windows (IBM Corp., Armonk, NY, United States) was used for the statistical evaluation of the research data. The measurable variables were presented as mean ± standard deviation, while the categorical variables were presented as number (*n*) and percentage (%). Spearman's rho correlation analysis was performed to determine the relationship between the variables. The hypotheses were bidirectional, and $P \leqslant 0.05$ was considered statistically

significant.

RESULTS

Demographics

A total of 70 patients from Diyarbakir, Batman, Mardin, and Sanliurfa were included in this prospective, multicenter study. The mean age of the patients was 37.1 years, with a predominance of males (49 patients, 70.0%).

Comparison of histopathologic evaluation and elastography

Two patients (2.9%) who underwent biopsy yielded insufficient tissue for histopathological evaluation. The concordance rate between elastography and histopathological results was 97.1% in the 68 patients who underwent biopsy ($P < 0.001$). In 2 cases (2.9%), the fibrosis value was higher than the liver biopsy result. In 66 patients (97.1%), the liver fibrosis score was $\geqslant 2$ or the hepatic activity index was $\geqslant 6$. According to these results, all patients began antiviral treatment because they met the reimbursement criteria in our country.

Evaluation of the liver before and after antiviral therapy

All patients began tenofovir disoproxil fumarate (TDF) treatment. Before treatment, 19 patients (27.1%) were diagnosed with MASLD and 6 patients (8.6%) with MASH. The mean CAP value of all patients, patients with MASLD, and patients with MASH was 224 dB/m, 275 dB/m, and 291 dB/m, respectively. The mean LSM was 7.2 kPa in the patients before antiviral therapy and 7.1 kPa at the 12-month follow-up. For the 2 patients with insufficient liver biopsy material, the mean LSM was 8.4. HBV-DNA was > 2000 IU/mL, mean ALT level was 55.1 IU/L, and mean low-density lipoprotein-cholesterol (LDL-C) level was 93.6 mg/dL in all patients (Table 1).

At the 12-month follow-up (Table 2), the MASLD rate decreased to 25.7% ($P = 0.064$). No change in the MASH rate was detected. HBV-DNA was undetectable in 95.6% of patients, and the ALT level was within normal ranges in 84.3% of patients.

Lipid profile and hepatosteatosis

Lipid profiles were evaluated before and after antiviral treatment. Triglycerides levels decreased (194.6 ± 40.2 mg/dL *vs.* 188.1 ± 31.9 mg/dL, $P = 0.069$), total cholesterol levels decreased (215.4 ± 40.2 mg/dL *vs.* 211.6 ± 31.1, $P = 0.058$), LDL-C levels decreased significantly (93.8 ± 21.6 *vs.* 75.6 ± 17.6, $P = 0.034$), and high-density lipoprotein-cholesterol (HDL-C) levels increased slightly (54.8 ± 8.2 *vs.* 55.1 ± 10.1, $P = 0.076$). Notably, only the decrease in the LDL-C level reached statistical significance. When patients with MASLD and MASH were evaluated separately, significant decreases in triglycerides, HDL-C, and LDL-C levels were found in patients with MASLD (Table 3).

DISCUSSION

Currently, high virologic response rates are achieved with high resistance barrier nucleos(t)ide antiviral therapies that suppress inflammation and reduce fibrosis progression.[2,17] Despite antiviral therapy, the risk of cirrhosis and HCC persists, and patients still require follow-up. In addition to viral injury, comorbid factors such as metabolic syndrome and MASLD/MASH play an important role in the progression of liver fibrosis and carcinogenesis. Although severe hepatosteatosis has been shown to accelerate the progression to fibrosis, the effect of milder steatosis is still unknown.[6,18] However, Con *et al.* observed that concomitant MASLD does not accelerate the progression to fibrosis in the short-term and medium-term in patients with CHB but without cirrhosis.[10]

In a very recent study, Huang *et al.* followed 11,502 treatment-naïve patients with CHB but without cirrhosis for 5.3 years.[19] They reported that patients in the metabolic dysfunction group were older and had lower HBV-DNA. The metabolic dysfunction group was also at higher risk for cirrhosis and cirrhosis complications. Newly occurring diabetes mellitus during follow-up also increased the risk of complications due to cirrhosis. Fatty liver was associated with a lower risk of cirrhosis and complications at 5 years. Among patients with fatty liver, those with MASLD showed a higher risk of cirrhosis than those without metabolic dysfunction.[19]

In patients with CHB, it is of great importance to evaluate liver fibrosis before initiating antiviral therapy to monitor the change in fibrosis during long-term follow-up. Biopsy is the gold standard for the evaluation of liver necroinflammation and fibrosis. However, there are several limitations including sampling errors, patient dissatisfaction, procedural difficulty, cost, bleeding and other complications, and differences in assessment.[1] Therefore, more studies and guidelines have been developed and suggested non-invasive tests and transient elastography as an alternative to guide treatment decisions before antiviral therapies and to monitor their efficacy afterwards.[1,20] Moreover, liver biopsy does not provide information on the status of fibrosis (*i.e.* progressing, regressing, or stable) and only provides instantaneous information.[21]

In a single-center study, the diagnostic efficacy of FibroScan® was compared to liver biopsy in 1185 patients with CHB.[14] A positive correlation was found

Table 1: Characteristics of patients with chronic hepatitis B

Variables	Results
Age, years, mean (SD, range)	37.1 (18.5, 22.0-62.0)
Underlying diseases *n*)	DM (5), HT (5)
Male, *n* (%)	49 (72.0)
ALT in IU/mL (mean ± SD)	55.1 ± 30.4
HBV-DNA, mean	$5.65 \times 10^7/mm^3$
Fibrosis ISHAK score, mean	2.1
LSM by FibroScan® in kPa, mean	7.2
CAP by Fibroscan® in dB/m, mean	224
Triglycerides in mg/dL	194.6 ± 40.2
Total cholesterol in mg/dL	215.4 ± 40.2
LDL-C in mg/dL	93.8 ± 21.6
HDL-C in mg/dL	54.8 ± 8.2
BMI, mean	26.7
Statin use, *n* (%)	2 (2.9)
Alcohol use*, *n* (%)	4 (5.9)

*Alcohol use was defined by consumption > 140 g/week for females and > 210 g/week for males. ALT: alanine aminotransferase; BMI: body mass index; CAP: controlled attenuation parameter; DM: diabetes mellitus; HDL-C: high-density lipoprotein-cholesterol; HT: hypertension; LDL-C: low-density lipoprotein-cholesterol; LSM: liver stiffness measurement; SD: standard deviation

Table 2: Change in baseline variables after 12 months of antiviral therapy

Baseline variable	Baseline	12-month follow-up	*P* value
MASLD, % *n*)	27.1 (19)	25.7 (18)	0.064
MASH, % *n*)	8.6 (6)	8.6 (6)	N/A
Mean ALT	54.9 IU/mL	43.1 IU/mL	< 0.001
Mean HBV-DNA	5.65×10^7	2.2×10^2	< 0.001
Mean CAP, *n* = 66	224.7	221.1	0.003
LSM by FibroScan® in kPa, mean	7.2	7.1	N/A
Triglycerides in mg/dL	194.6 ± 40.2	188.1 ± 31.9	0.069
Total cholesterol in mg/dL	215.4 ± 40.2	211.6 ± 31.1	0.058
LDL-C in mg/dL	93.8 ± 21.6	75.6 ± 17.6	0.034
HDL-C in mg/dL	54.8 ± 8.2	55.1 ± 10.1	0.076

ALT: alanine aminotransferase; CAP: controlled attenuation parameter; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; LSM: liver stiffness measurement; MASH: metabolic dysfunction-associated steatohepatitis; MASLD: metabolic dysfunction-associated fatty liver disease; N/A: not available

between the degree of inflammation and LSM values. Liver inflammation can be evaluated as well as liver fibrosis by FibroScan®.[14] Moreover, a recent meta-analysis showed that FibroScan® has good sensitivity and specificity for the detection of steatosis and fibrosis.[22] The authors also argued that FibroScan® is cost-effective, reproducible, and useful for patient follow-up. In another study, FibroScan® was also used validation of tests used in the diagnosis of fatty liver disease.[23] The use of FibroScan® in the assessment of MASLD/MASH in many patient groups, including CHC, HIV-infected, diabetes and obstructive sleep apnea, indicates its increasing use worldwide.[24–27]

In our country, the reimbursement system for oral antiviral treatment is like the criteria in the AASLD/EASL and APASL guidelines.[2,28,29] Oral antiviral treatment requirements are generally covered by our insurance system. The most patients at follow-up do not want to undergo a repeat liver biopsy. Therefore, at the 12-month follow-up, we only evaluated the effect of antiviral therapy by Fibroscan®. Moreover, we showed that the correlation between biopsy and Fibroscan® was quite high before therapy. We found that 27.1% of the patients had MASLD and 8.6% had MASH. The mean CAP values for all patients, patients with MASLD, and patients with MASH were 224 dB/m, 275 dB/m, and 291 dB/m, respectively, with a mean LSM level of 7.2

Table 3: Lipid profile before and after 12-month treatment of tenofovir disoproxil fumarate in chronic hepatitis B patients with metabolic dysfunction-associated fatty liver disease and metabolic dysfunction-associated steatohepatitis

Lipid profile	Baseline	12-month follow-up	*P* value
Patients with MASLD			
Triglycerides in mg/dL	224.4 ± 22.3	215.7 ± 17.8	0.041
Total cholesterol in mg/dL	228.8 ± 29.3	225.7 ± 21.1	0.072
LDL-C in mg/dL	98.6 ± 19.3	81.9 ± 15.8	0.034
HDL-C in mg/dL	51.2 ± 9.1	53.8 ± 8.4	0.033
Patients with MASH			
Triglycerides in mg/dL	228.4 ± 28.4	227.7 ± 27.1	0.081
Total cholesterol in mg/dL	226.1 ± 23.8	225.9 ± 20.9	0.078
LDL-C in mg/dL	99.5 ± 16.6	96.9 ± 13.6	0.094
HDL-C in mg/dL	50.9 ± 8.1	51.6 ± 7.8	0.088

HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; MASH: metabolic dysfunction-associated steatohepatitis; MASLD: metabolic dysfunction-associated fatty liver disease

kPa. Con *et al.* reported that LSM was 15% higher in patients with CHB and MASLD compared to those without MASLD.[10] Moreover, LSM values increased as hepatis B viral load increased. They also showed that LSM values decreased in patients with and without MASLD during follow-up after therapy.

We observed a decrease in the MASLD rate after 12 months of antiviral treatment, but the rate of MASH did not change. Several studies have reported a paradox that concurrent hepatic steatosis appears to provide viral suppression and increase the hepatitis B surface antigen seroconversion rate.[7,9,18] However, it is generally accepted that hepatic steatosis causes or triggers fibrosis.[6] These conflicting findings suggest a complex association with CHB, especially after the redefinition of fatty liver as MASLD. Even if the presence of hepatosteatosis leads to reduced viral activity and regression of liver injury, the presence of metabolic risk factors such as diabetes may increase the risk of HCC.[30,31]

A recent study reported that 483 of 1613 patients with CHB had MASLD (29.9%), and the cumulative incidence of HCC was higher in those with MASLD in the 5.02-year follow-up period.[32] Similarly, in a health screening program with a large number of participants (336,866 adults, aged ⩾ 30 years), 36.4% were diagnosed with MASLD, 14.6% had CHB, 1.1% had chronic hepatitis C (CHC), and 0.3% had CHB and CHC coinfection. The presence of MASLD in patients with CHB or CHC who received antivirals during follow-up was reported to be associated with an increased risk of cirrhosis and HCC.[33] However, the risk of cirrhosis and HCC was higher in those with only CHB or CHC than in those with MASLD alone. The authors concluded that antiviral treatment of chronic viral hepatitis had priority before addressing MASLD.[33]

Liver transplantation may be unique option because of the bad scenarios mentioned above. If MASLD/MASH is present before transplantation, it may recur or develop *de novo*. In one study, the diagnosis of recurrent MASH by FibroScan® after liver transplantation was compared with liver biopsy. In this study, a strong correlation was shown when post-transplant LSM values were < 8 kPa. They concluded that FibroScan® could be an effective non-invasive tool to stage liver fibrosis recurrence among patients transplanted for MASH cirrhosis, and specifically to screen for those at no need of biopsy.[34]

It is noteworthy that patients with MASLD/MASH in our study had higher lipid levels. However, there appeared to be a mild lipid profile abnormality in all patients. It has been suggested that dyslipidemia is indirectly related to the development of HCC through hepatic fibrosis in patients with chronic viral hepatitis. It is also well known that dyslipidemia causes steatohepatitis, and severe hepatic steatosis increases the risk of liver fibrosis in patients with CHB.[19,35] Even in one study, dietary inflammatory index in relation to the progression of hepatic steatosis and liver fibrosis was evaluated by FibroScan®.[36] There are several conflicting results with FibroScan® measurements in obese individuals with more accurate results in those with lower BMI.[37,38] In a recent study, intraoperative liver biopsy was compared with FibroScan® in patients undergoing bariatric surgery and acceptable data were obtained. It was shown that the data were better in patients with BMI < 44.4 kg/m^2.[39]

In a recent network meta-analysis, it was reported that TDF may reduce the levels of lipid profiles, especially total cholesterol levels. This effect was not evident among the patients with CHB receiving tenofovir alafenamide, entecavir, or no treatment.[40] When all

patients in our study were evaluated at the 12-month follow-up during TDF treatment, only LDL-C levels significantly decreased, whereas triglycerides, HDL-C, and LDL-C levels decreased after the subgroup analysis of patients with MASLD. This improvement in lipid profile may be because of TDF. Considering its renal toxicity and effects on bone mineral density, TDF should be used with caution, especially in elderly patients. However, TDF may be preferred in patients with an impaired lipid profile and those at risk of atherosclerotic heart disease.[40]

The advantages of this study included the prospective, multicenter design. All patients also underwent biopsy at baseline. The limitations of the study were the small number of patients who represented only one region of the country, and the short follow-up period. The 24th month follow-up of the patients and their measurements by FibroScan® are ongoing.

In conclusion, the association of metabolic disfunction and MASLD/MASH in patients with CHB is increasing. These risk factors should be proactively investigated in treatment-naïve patients during follow-up. FibroScan® is a useful, non-invasive alternative to biopsy for the diagnostic evaluation and treatment follow-up of these patients.

DECLARATIONS

Acknowledgments
We thank Nobel Pharmaceuticals and Southeast Neurology and Infectious Diseases Society for financial support.

Author contributions
Celen MF served as the principal investigator, constructed the hypothesis/idea of the research, wrote the manuscript, prepared the application for the Ethics Committee, and performed the Fibroscan® measurements; Mermutluoglu C, Akgül F, Cakmak P, Cakirca TD collected the data, took responsibility for the patient follow-up, and wrote the manuscript; Yildiz I performed the statistical analysis and writing of the manuscript; Tasova Y and Bayindir Y constructed the hypothesis/idea of the research, wrote the manuscript, and prepared the application for the Ethics Committee; All authors read and approved the final manuscript.

Source of fund
Nobel Pharmaceuticals, and Southeast Neurology and Infectious Diseases Society

Use of large language models, AI and machine learning tools
None declared.

Informed consent
Written informed consent was obtained from all participants.

Conflict of interest
All the authors report no relevant conflicts of interest for this article.

Data sharing statement
Technical appendix, statistical code, and dataset available from the corresponding author at yasarb44@hotmail.com.

REFERENCES

1. Vittal A, Ghany MG. WHO Guidelines for Prevention, Care and Treatment of Individuals Infected with HBV: A US Perspective. Clin Liver Dis 2019;23:417-432
2. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67:370-398
3. Global hepatitis report 2024: action for access in low- and middle-income countries. Geneva: World Health Organization; 2024.
4. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol 2023;79:1542-1556
5. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 1999;116:1413-1419
6. Seto WK, Hui RWH, Mak LY, Fung J, Cheung KS, Liu KSH, Wong DK, et al. Association between hepatic steatosis, measured by controlled attenuation parameter, and fibrosis burden in chronic hepatitis B. Clin Gastroenterol Hepatol 2018;16:575-583.e2
7. Wang L, Wang Y, Liu S, Zhai X, Zhou G, Lu F, et al. Nonalcoholic fatty liver disease is associated with lower hepatitis B viral load and antiviral response in pediatric population. J Gastroenterol 2019;54:1096-1105
8. Hui RWH, Seto WK, Cheung KS, Mak LY, Liu KSH, Fung J, et al. Inverse relationship between hepatic steatosis and hepatitis B viremia: Results of a large case-control study. J Viral Hepat 2018;25:97-104
9. Hu D, Wang H, Wang H, Wang Y, Wan X, Yan W, et al. Non-alcoholic hepatic steatosis attenuates hepatitis B virus replication in an HBV-immunocompetent mouse model. Hepatol Int 2018;12:438-446
10. Con D, Tu S, Clayton-Chubb D, Lubel JS, Nicoll AJ, Sawhney R, et al. Effect of concurrent metabolic dysfunction-associated steatotic liver disease on serial non-invasive fibrosis markers in chronic hepatitis B. Dig Dis Sci 2024;69:1496-1506
11. Wang T, Xi Y, Raji A, Crutchlow M, Fernandes G, Engel SS, et al. Overall and subgroup prevalence of non-alcoholic fatty liver disease and prevalence of advanced fibrosis in the United States: An updated national estimate in National Health and Nutrition Examination Survey (NHANES) 2011-2018. Ann Hepatol 2024;29:101154
12. Friedman LS. Controversies in liver biopsy: who, where, when, how, why? Curr Gastroenterol Rep 2004;6:30-36
13. Martonik D, Wandałowicz A, Supronowicz Ł, Panasiuk A, Parfieniuk-Kowerda A, Flisiak R. Shear-wave elastography for evaluation of hepatic stiffness in chronic viral hepatitis B and C. Clin Exp Hepatol 2023;9:179-186
14. Jiang K, Zhang L, Li J, Hu H, Huang Q, Qiu T, et al. Diagnostic efficacy of FibroScan for liver inflammation in patients with chronic hepatitis B: a single-center study with 1185 liver biopsies as controls.

BMC Gastroenterol 2022;22:37

15. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. J Hepatol 2021;75:659-689
16. Jung KS, Kim SU, Ahn SH, Park YN, Kim DY, Park JY, et al. Risk assessment of hepatitis B virus-related hepatocellular carcinoma development using liver stiffness measurement (FibroScan). Hepatology 2011;53:885-894
17. Li J, Gordon SC, Rupp LB, Zhang T, Trudeau S, Holmberg SD, et al. Long-term progression of viral load and serum markers of fibrosis among treated and untreated patients with chronic hepatitis B. J Gastroenterol Hepatol 2017;32:1250-1257
18. Mak LY, Hui RW, Fung J, Liu F, Wong DK, Cheung KS, et al. Diverse effects of hepatic steatosis on fibrosis progression and functional cure in virologically quiescent chronic hepatitis B. J Hepatol 2020; 73: 800-806
19. Huang SC, Su TH, Tseng TC, Liao SH, Hsu SJ, Hong CM, et al. Pre-existing and new-onset metabolic dysfunctions ıncrease cirrhosis and ıts complication risks in chronic hepatitis B. Am J Gastroenterol 2025;120:401-409
20. Li Q, Chen L, Zhou Y. Changes of FibroScan, APRI, and FIB-4 in chronic hepatitis B patients with significant liver histological changes receiving 3-year entecavir therapy. Clin Exp Med 2018;18:273-282
21. European Association for Study of Liver; Asociacion Latinoamericana para el Estudio del Higado. EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 2015;63:237-264
22. Xu X, Jin J, Liu Y. Performance of FibroScan in grading steatosis and fibrosis in patients with nonalcoholic fatty liver disease: A meta-analysis. Arab J Gastroenterol 2023;24:189-197
23. Jeong S, Park SJ, Na SK, Park SM, Song BC, Oh YH. Validity of fatty liver prediction scores for diagnosis of fatty liver by Fibroscan. Hepatobiliary Pancreat Dis Int 2024;23:353-360
24. Kalopitas G, Arvanitakis K, Tsachouridou O, Malandris K, Koufakis T, Metallidis S, et al. Metabolic Dysfunction-Associated Steatotic Liver Disease in People Living with HIV-Limitations on Antiretroviral Therapy Selection. Life (Basel) 2024;14
25. Ko MY, Hsu YC, Yen HH, Huang SP, Su PY. The effects of pangenotypic direct-acting antiviral therapy on lipid profiles and ınsulin resistance in chronic hepatitis C patients. Viruses 2025;17
26. Guido D, Cerabino N, Di Chito M, Di Stasi V, De Nucci S, Shahini E, et al. Association between liver steatosis, fibrosis, and the onset of type 2 diabetes in overweight individuals: A fibroscan-based study in Southern Italy. Diabetes Res Clin Pract 2024;218:111911
27. Parchani A, Gupta R, Kant R, Saini LK, Gupta R. Evaluation of hepatic steatosis and fibrosis using transient elastography in patients with obstructive sleep apnea. J Clin Exp Hepatol 2024;14:101289
28. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018;67:1560-1599
29. Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HL, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. Hepatol Int 2016;10:1-98
30. Wang C, Wang X, Gong G, Ben Q, Qiu W, Chen Y, et al. Increased risk of hepatocellular carcinoma in patients with diabetes mellitus: a systematic review and meta-analysis of cohort studies. Int J Cancer 2012;130:1639-1648
31. Tourkochristou E, Assimakopoulos SF, Thomopoulos K, Marangos M, Triantos C. NAFLD and HBV interplay - related mechanisms underlying liver disease progression. Front Immunol 2022;13:965548
32. Lin M, Gao B, Peng M, Chen X, Xiao H, Shi M, et al. Metabolic dysfunction-associated steatotic liver disease increases hepatocellular carcinoma risk in chronic hepatitis B patients: a retrospective cohort study. Front Physiol 2024;15:1347459
33. Lee MH, Chen YT, Huang YH, Lu SN, Yang TH, Huang JF, et al. Chronic viral hepatitis B and C Outweigh MASLD in the associated risk of cirrhosis and HCC. Clin Gastroenterol Hepatol 2024;22:1275-1285.e2
34. Martínez-Arenas L, Vinaixa C, Conde I, Lorente S, Díaz-Fontenla F, Marques P, et al. FibroScan compared to liver biopsy for accurately staging recurrent hepatic steatosis and fibrosis after transplantation for MASH. Liver Int 2024; 44: 3174-3182
35. Diao Y, Tang J, Wang X, Deng W, Tang J, You C. Metabolic syndrome, nonalcoholic fatty liver disease, and chronic hepatitis b: a narrative review. Infect Dis Ther 2023;12:53-66
36. Miryan M, Rashid SA, Navashenaq JG, Soleimani D, Nematy M, Moludi J. Dietary inflammatory index in relation to the progression of hepatic steatosis and liver fibrosis: evaluation by elastography/ Fibroscan. BMC Gastroenterol 2024;24:128
37. Mikolasevic I, Orlic L, Franjic N, Hauser G, Stimac D, Milic S. Transient elastography (FibroScan(®)) with controlled attenuation parameter in the assessment of liver steatosis and fibrosis in patients with nonalcoholic fatty liver disease - Where do we stand? World J Gastroenterol 2016;22:7236-7251
38. Sun J, Yan C, Wen J, Wang F, Wu H, Xu F. Association between different obesity patterns and the risk of NAFLD detected by transient elastography: a cross-sectional study. BMC Gastroenterol 2024;24:221
39. Eilenberg M, Munda P, Stift J, Langer FB, Prager G, et al. Accuracy of non-invasive liver stiffness measurement and steatosis quantification in patients with severe and morbid obesity. Hepatobiliary Surg Nutr 2021;10:610-622
40. Tong K, Chen M, Wang D, Dai H, Peng J, Zhang J, Zhou J, Chang Y, Huang W. Effects of first-line nucleot(s)ide analogues on lipid profiles in patients with chronic hepatitis B: a network meta-analysis. Eur J Clin Pharmacol 2024; 80: 335-354