



The role of FibroScan in the era of metabolic (dysfunction)-associated fatty liver disease

 Yusuf Yilmaz^{1,2},  Eda Kaya^{3,4}

¹Department of Gastroenterology, Recep Tayyip Erdogan University School of Medicine, Rize, Türkiye; ²Institute of Gastroenterology, Marmara University, Istanbul, Türkiye; ³Section of Hepatology and Gastroenterology; and ⁴Department of Medicine, Universitätsklinikum Knappschafts Krankenhaus Bochum, Ruhr University Bochum, Bochum, Germany

Among chronic liver conditions, metabolic (dysfunction)-associated fatty liver disease (MAFLD) ranks as the most frequent. With a worldwide prevalence of 37%, the global burden of MAFLD is large and growing.^[1] Approximately 45% of the Turkish population meets the diagnostic criteria for MAFLD,^[2] which are based on detection of liver steatosis by imaging techniques, blood biomarkers or non-invasive scores, or by liver histology in addition to one of the following three criteria: Overweight or obesity, presence of Type 2 diabetes, or evidence of metabolic dysregulation.^[3]

After diagnosis, the clinical trajectory of patients with MAFLD is a long-life journey that starts from triaging the severity of liver disease to the implementation of treatment and follow-up surveillance. Being the key prognostic determinant, timely detection and accurate staging of hepatic fibrosis are vital for prioritizing treatment and improving outcomes.^[4] According to current guidelines, this overarching goal should be achieved through a stepwise approach aimed at increasing the diagnostic and predictive certainty. Specifically, the first step is based on the use of simple compound surrogates calculated from routine clinical and laboratory parameters – including the fibrosis-4 index and non-alcoholic fatty liver disease (NAFLD) fibrosis score. This should be followed by second-line FibroScan examinations whenever patients are classified at high or intermediate risk of advanced fibrosis during the preceding step.^[5,6] This approach is expected to avoid unnecessary liver biopsies – ultimately reducing the economic burden of MAFLD on health-care systems.^[7,8]

Given the key role played by overweight or obesity in the pathogenesis of MAFLD, the concomitant presence of the two conditions poses special challenges. A recent meta-analysis involving more than two million subjects from the general population reported that approximately 50% of those being overweight or obese met the diagnostic criteria for MAFLD.^[9] Considering that obesity is a risk factor for the development of advanced fibrosis, there is an urgent need to improve

early detection and diagnosis of this condition in the obese population.^[10] At present, FibroScan parameters are among the best established imaging biomarkers of hepatic fibrosis and steatosis.^[11] However, there are some methodological issues to be considered when FibroScan is performed in obese individuals. Due to the increased distance between the skin and liver capsule, the examination should be conducted with a specific XL probe. This approach is valuable as it allows successful measurements in up to 97% of cases, although some operator-dependent differences still exist.^[12,13]

Due to its widespread availability and low costs, abdominal ultrasonography remains the most extensively used imaging modality for the identification of hepatic steatosis in patients with MAFLD.^[14] However, its clinical value in the detection of mild-to-moderate steatosis (<30%) is limited and more sensitive methods – including controlled attenuation parameter obtained from FibroScan – should be recommended.^[15] Another advantage of FibroScan over abdominal ultrasonography is that information concerning both steatosis and fibrosis can be simultaneously obtained. Finally, FibroScan data have high agreement with liver biopsy findings across different fibrosis stages.^[16,17]

Although advanced fibrosis is the most robust prognostic determinant of liver-related, cardiovascular, and overall mortality,^[4] clinical outcomes in MAFLD can also be affected by patient age and Type 2 diabetes mellitus.^[18] In addition, while FibroScan data are considered among the best standards in the field of non-invasive hepatic diagnostics, the presence of potential bias and confounders (e.g., obesity and operator experience) is fairly common in the clinical setting. In this scenario, models combining both clinical and FibroScan variables are expected to outperform FibroScan alone in the prediction of fibrosis. Among them, Agile 3+ and Agile 4 have been developed for optimizing the identification of advanced fibrosis and cirrhosis, respectively.^[19] These scoring systems – wherein liver stiffness measurements are combined with clinical and laboratory parameters (e.g., age, sex, alanine transaminase, aspartate transaminase, platelet count, and diabetes status) – have been recently shown to reflect health-related quality of life in patients with NAFLD.^[20]

In conclusion, the detection of hepatic fibrosis and steatosis by means of FibroScan bears great relevance in the clinical management of patients with MAFLD. According to recently proposed guidelines, this non-invasive imaging modality ought to play an important supportive role with respect to prognostic stratification. Using a combination of liver stiffness measurements and clinical parameters, recent studies have also been able to devise and validate refined prognostic scores that may be applied to patients in need of close surveillance protocols.

How to cite this article: Yilmaz Y, Kaya E, Karcaaltincaba M. The role of FibroScan in the era of metabolic (dysfunction)-associated fatty liver disease. *Hepatology Forum* 2023; 4(2):I-II.

Received: November 20, 2022; **Accepted:** November 21, 2022; **Available online:** May 18, 2023

Corresponding author: Yusuf Yilmaz; Recep Tayyip Erdogan Universitesi Tip Fakultesi, Gastroenteroloji Anabilim Dalı, Rize, Türkiye
Phone: +90 533 440 39 95; **e-mail:** dryusufyilmaz@gmail.com



OPEN ACCESS
This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Hepatology Forum - Available online at www.hepatologyforum.org



Conflict of Interest: Yusuf Yilmaz has served as consultant to Cymabay, Zydus, Novo, Nordisk, and Echosens. Eda Kaya have no conflict of interest to disclose.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Kaya E, Yilmaz Y. Epidemiology, natural history, and diagnosis of metabolic dysfunction-associated fatty liver disease: a comparative review with nonalcoholic fatty liver disease. *Ther Adv Endocrinol Metab* 2022;13:20420188221139650. [\[CrossRef\]](#)
2. Yilmaz Y, Yilmaz N, Ates F, Karakaya F, Gokcan H, Kaya E, et al. The prevalence of metabolic-associated fatty liver disease in the Turkish population: A multicenter study. *Hepatol Forum* 2021;2(2):37-42. [\[CrossRef\]](#)
3. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol* 2020;73(1):202-209. [\[CrossRef\]](#)
4. Sanyal AJ, Van Natta ML, Clark J, Neuschwander-Tetri BA, Diehl A, Dasarathy S, et al; NASH Clinical Research Network (CRN). Prospective Study of Outcomes in Adults with Nonalcoholic Fatty Liver Disease. *N Engl J Med* 2021;385(17):1559-1569. [\[CrossRef\]](#)
5. Eslam M, Sarin SK, Wong VW, Fan JG, Kawaguchi T, Ahn SH, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Hepatol Int* 2020;14(6):889-919. [\[CrossRef\]](#)
6. Yilmaz Y, Zeybel M, Adali G, Cosar AM, Serteser E, Gokcan H, et al. TASA Practice Guidance on the Clinical Assessment and Management of Patients with Nonalcoholic Fatty Liver Disease. *Hepatol Forum* 2023;(Suppl 1):1-32.
7. Jafarov F, Kaya E, Bakir A, Eren F, Yilmaz Y. The diagnostic utility of fibrosis-4 or nonalcoholic fatty liver disease fibrosis score combined with liver stiffness measurement by fibroscan in assessment of advanced liver fibrosis: a biopsy-proven nonalcoholic fatty liver disease study. *Eur J Gastroenterol Hepatol* 2020;32(5):642-649. [\[CrossRef\]](#)
8. Younossi ZM, Corey KE, Alkhoury N, Noureddin M, Jacobson I, Lam B, et al; US Members of the Global Nash Council. Clinical assessment for high-risk patients with non-alcoholic fatty liver disease in primary care and diabetology practices. *Aliment Pharmacol Ther* 2020;52(3):513-526. [\[CrossRef\]](#)
9. Liu J, Ayada I, Zhang X, Wang L, Li Y, Wen T, et al. Estimating global prevalence of metabolic dysfunction-associated fatty liver disease in overweight or obese adults. *Clin Gastroenterol Hepatol* 2022;20(3):e573-e582.
10. Seval GC, Kabacam G, Yakut M, Seven G, Savas B, Elhan A, Cinar K, Idilman R. The natural course of non-alcoholic fatty liver disease. *Hepatol Forum* 2020;1(1):20-24. [\[CrossRef\]](#)
11. Oeda S, Takahashi H, Imajo K, Seko Y, Ogawa Y, Moriguchi M, et al. Accuracy of liver stiffness measurement and controlled attenuation parameter using FibroScan® M/XL probes to diagnose liver fibrosis and steatosis in patients with nonalcoholic fatty liver disease: a multicenter prospective study. *J Gastroenterol* 2020;55(4):428-440. [\[CrossRef\]](#)
12. Avcu A, Kaya E, Yilmaz Y. Feasibility of fibroscan in assessment of hepatic steatosis and fibrosis in obese patients: Report from a general internal medicine clinic. *Turk J Gastroenterol* 2021;32(5):466-472. [\[CrossRef\]](#)
13. Zhang X, Wong GL, Wong VW. Application of transient elastography in non-alcoholic fatty liver disease. *Clin Mol Hepatol* 2020;26(2):128-141. [\[CrossRef\]](#)
14. Salmi A, di Filippo L, Ferrari C, Frara S, Giustina A. Ultrasound and FibroScan® Controlled Attenuation Parameter in patients with MAFLD: head to head comparison in assessing liver steatosis. *Endocrine* 2022;78(2):262-269. [\[CrossRef\]](#)
15. Yilmaz Y, Ergelen R, Akin H, Imeryuz N. Noninvasive detection of hepatic steatosis in patients without ultrasonographic evidence of fatty liver using the controlled attenuation parameter evaluated with transient elastography. *Eur J Gastroenterol Hepatol* 2013;25(11):1330-1334. [\[CrossRef\]](#).
16. Siddiqui MS, Vuppalandi R, Van Natta ML, Hallinan E, Kowdley KV, Abdelmalek M, et al. Vibration-controlled transient elastography to assess fibrosis and steatosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol* 2019;17(1):156-163.e2. [\[CrossRef\]](#)
17. Aykut UE, Akyuz U, Yesil A, Eren F, Gerin F, Ergelen R, et al. A comparison of FibroMeter™ NAFLD Score, NAFLD fibrosis score, and transient elastography as noninvasive diagnostic tools for hepatic fibrosis in patients with biopsy-proven non-alcoholic fatty liver disease. *Scand J Gastroenterol* 2014;49(11):1343-1348. [\[CrossRef\]](#)
18. Huang DQ, El-Serag HB, Loomba R. Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol* 2021;18(4):223-238. [\[CrossRef\]](#)
19. Sanyal AJ, Foucquier J, Younossi ZM, Harrison SA, Newsome PN, Chan WK, et al. Enhanced diagnosis of advanced fibrosis and cirrhosis in individuals with NAFLD using FibroScan-based Agile scores. *J Hepatol* 2023;78(2):247-259. [\[CrossRef\]](#)
20. Yilmaz Y, Toraman AE, Alp C, Doğan Z, Keklikkiran C, Stepanova M, et al. Impairment of patient-reported outcomes among patients with non-alcoholic fatty liver disease: a registry-based study. *Aliment Pharmacol Ther* 2023;57(2):215-223. [\[CrossRef\]](#)