Research Article

Comparison of invasive and non-invasive tests

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Performance of non-invasive fibrosis markers in biopsy-proven liver disorders

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Abstract

Background and Aim: The primary aim of this study was to investigate the concordance of Transient Elastography FibroScan® (FS) measurements, Fibrosis-4 (FIB-4), and the Aspartate Aminotransferase to Platelet Ratio Index (APRI) scores with each other and with liver biopsies in predicting histological fibrosis.

Materials and Methods: In this single-center, cross-sectional, retrospective collected data cohort study spanning seven consecutive years, simultaneous FS measurements, FIB-4, and APRI scores of 778 patients with different diagnoses who had undergone liver biopsy were evaluated.

Results: A total of 417 (53.6%) of the patients were female. The median age was 51 years. The diagnoses were HBV (n=228), metabolic dysfunction-associated steatotic liver disease (MASLD) (n=185), HCV (n=58), cryptogenic (n=53), primary biliary cholangitis (n=40), autoimmune hepatitis (AIH) (n=28), overlap syndrome (OS) (n=23), multiple diagnoses (n=42), and other diagnoses (n=83). All three methods showed a strong correlation with histological fibrosis, and FS demonstrated a statistically significantly superior relationship compared to FIB-4 and APRI. In AIH and OS, FIB-4 and APRI scores do not show a consistent increase with histological stage; however, FS does. In MASLD, all three methods correlate with histologic stage, but FS measurements appear significantly superior.

Conclusion: Although FIB-4, APRI, and FS correlate well with histological fibrosis, especially in MASLD, evaluation with FS, if available, should be preferred. In the evaluation of fibrosis in AIH and OS, laboratory-based indicators should be avoided.

Keywords: FIB-4; liver biopsy; transient elastography.

Introduction

Percutaneous liver biopsy is a method that continues to be used in the staging of chronic liver diseases, determining treatment indications, assessing treatment response, and identifying the etiology of acute liver injury. However, due to its invasive nature, percutaneous liver biopsy has low repeatability because of risks such as bleeding, pain, bile peritonitis, pneumothorax, hemothorax, bacteremia, and sepsis.[1] Due to these complication risks, non-invasive serum parameters and imaging methods have been investigated, especially in the follow-up of diseases requiring repeated biopsies. One of the most widely accepted and extensively studied methods among these is transient elastography.

Transient elastography (FibroScan®) (FS) has gained widespread use worldwide as a validated method for predicting fibrosis. FS numerically measures the elasticity of soft tissues, and as fibrosis increases in the tissue of interest, the measured value by the device also increases, reflecting the increased stiffness of the tissue. It has been reported that the volume of liver tissue assessed for stiffness measurement by FS is approximately 100 times larger than the tissue obtained through liver biopsy. Therefore, this method is suggested to better reflect the liver parenchyma. FS is a painless procedure that takes only a few minutes.[2]

In adults, it is generally accepted that age and gender do not significantly affect the measurement.[3] However, some studies report a difference. The normal transient elastography value in healthy people in Europe was 5.81±1.54 [range, 3.8–8.0] kPa in males and 5.23±1.59 [range, 3.3–7.8] kPa in females.[4] In two different studies conducted in Asia, normal values in healthy people were found in the range of 2.0–7.1 and 3.9–5.3 kPa.[5,6]

Chronic liver diseases include viral hepatitis (hepatitis B [HBV], hepatitis C [HCV], hepatitis D [HDV]), metabolic dysfunction-associated fatty liver disease (MASLD), autoimmune hepatitis (AIH), primary biliary cholangitis, primary sclerosing cholangitis, overlap syndromes (OS), and Wilson's disease.[7] In these diseases, normal values determined by elastography show minimal differences. According to the European Association for the Study of the Liver (EASL) guidelines, the threshold value accepted for indicating significant fibrosis in chronic HBV patients with normal ALT levels is 9 kPa, whereas for patients with elevated ALT levels (less than 5 times the upper limit of normal), it is 12 kPa.[8] In 327 patients with chronic hepatitis C, it was shown that elastography can accurately diagnose significant fibrosis with a cut-off value of 8.7 kPa and cirrhosis with a cut-off value of 14.5 kPa.[9]

Fibrosis-4 (FIB-4) and the Aspartate Aminotransferase to Platelet Ratio Index (APRI) are simple serological markers used in the assessment

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of liver fibrosis. The necessary components for these scores are age, Aspartate Aminotransferase (AST) level, Alanine Aminotransferase (ALT) level, and platelet count. (APRI=[(AST level/Upper Limit of Normal [ULN])/platelet count (10^9/L)]×100; FIB-4=[age×AST/platelet count (10^9/L)×√ALT].

The primary aim of this study was to investigate the concordance of FS measurements, FIB-4, and APRI scores with each other and with liver biopsies in predicting histological fibrosis. Secondary objectives were to determine the correlation of each method with histological fibrosis in different diseases, to compare the correlation values of the methods for different diseases, and to provide recommendations on whether serological markers can substitute for FS in centers where FS is not available.

Materials and Methods

Liver biopsies performed percutaneously at a single center between June 2014 and December 2020 were retrospectively reviewed. Before performing a liver biopsy, all patients were informed about the procedure and potential complications by the performing physician, and written informed consent regarding the procedure was obtained from the patients. Before the procedure, patients' complete blood count and coagulation parameters were assessed. If these values were not suitable for biopsy, appropriate replacements were made, aiming for a platelet count above 100,000×10^9/L and INR below 1.5, following which the biopsy was performed.

The area for biopsy was marked using ultrasound guidance. After local anesthesia with 1% lidocaine was administered, a 17-gauge Menghini-type liver biopsy needle (Hepafix®, B. Braun Melsungen AG, 34209 Melsungen, Germany) was used to enter through the previously marked intercostal space and complete the biopsy. Patients were monitored in the clinic for at least 4 hours, and vital signs were observed. If there was suspicion of complications, patients were admitted to the Gastroenterology ward and monitored for at least 24 hours.

Data recorded included date of birth, gender, pathological diagnosis, indication for biopsy (if due to chronic liver disease), histological activity index (grade), fibrosis grade (stage), AST, ALT, platelet count, INR values, and the year of liver biopsy. Diagnoses were categorized as hepatitis B virus (HBV), hepatitis C virus (HCV), autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), metabolic dysfunction-associated steatotic liver disease (MASLD), malignant lesion, overlap syndrome, normal liver tissue, inadequate liver biopsy, other reasons, cases with unclear etiology, cases with multiple etiologies, and nodular regenerative hyperplasia. Other causes included Wilson's disease, hemochromatosis, granulomatous hepatitis, graft-versus-host disease, vascular pathologies, Dubin-Johnson syndrome, toxic hepatitis, obstructive biliary pathologies, acute and chronic rejections, primary sclerosing cholangitis, autoimmune cholangitis, congenital hepatic fibrosis, and vanishing bile duct syndrome.

In patients whose liver fibrosis was evaluated with the FS device, in use since December 2014, and who had simultaneously undergone liver biopsy, the correlation between the fibrosis values obtained by FS, the fibrosis values obtained by biopsy, and the FIB-4 and APRI scores calculated from blood samples taken simultaneously were investigated.

The following formulas were used:

FIB-4=(AST×Age)/(Platelet×√ALT);

APRI=(AST/[AST ULN])/Platelet×100.

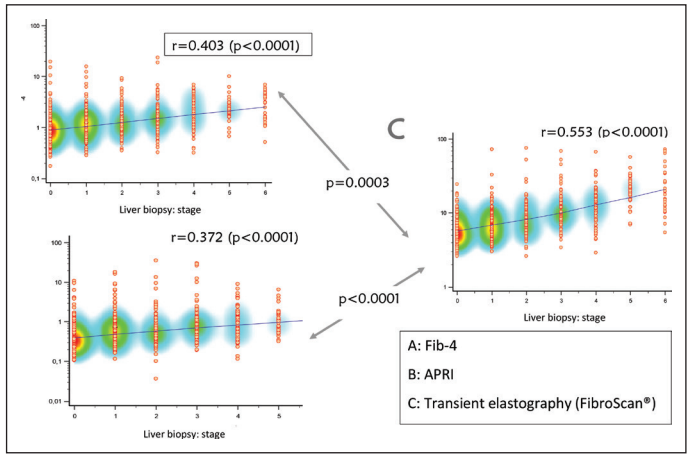

Figure 1. Correlation of non-invasive fibrosis markers with the liver biopsy fibrosis stage.

FS Test Protocol

The FS 502 (Echosens, Paris, France) test was performed on an empty stomach in the morning or at least 4 hours after food intake. FS was performed independently by two operators with relevant experience in our department, each of whom had successfully performed the procedure more than 500 times. The median value of 10 effective measurements was obtained in each test.[10] The liver stiffness measurement (LSM) results were expressed in kilopascals (kPa). In the present study, the operators adhered to the following reliability criteria:[11] the ratio of the interquartile range (IQR) to the median (M) (IQR/M) was less than 0.30, with less than 0.10 being regarded as optimal, and a success rate no less than 60%, with over 90% regarded as optimal.

Patients with ascites, those with HCC, insufficient biopsy samples, inadequate FS measurements, and those lacking the necessary parameters for calculating FIB-4 and APRI scores were excluded from the study.

Fibrosis in liver biopsy was evaluated according to the Ishak score. According to the Ishak scoring system, no fibrosis was assigned a score of 0; some portal fibrosis with or without fibrous septa was assigned a score of 1; portal fibrosis with or without fibrous septa was assigned a score of 2; portal fibrosis with occasional portal-to-portal bridging was assigned a score of 3; portal fibrosis with marked portal-to-portal bridging and portal-to-central bridging was assigned a score of 4; marked portal-to-portal bridging and portal-to-central bridging with occasional nodules (incomplete cirrhosis) was assigned a score of 5; and probable or definite cirrhosis was assigned a score of 6.[12] Fibrosis values of patients with steatotic liver disease were adjusted accordingly.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 22.0, SPSS Inc., Chicago, IL). The normality of the data was analyzed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed data were presented as mean and standard deviation, while non-normally distributed data were presented as median, minimum, and maximum values.

In the general population and various disease groups, the correlation of FS, FIB-4, and APRI measurements with histological fibrosis stage was investigated using the Spearman rank correlation test. The difference in correlation levels between different groups was compared using the Z-test analysis. MedCalc® Statistical Software version 19.8 (MedCalc

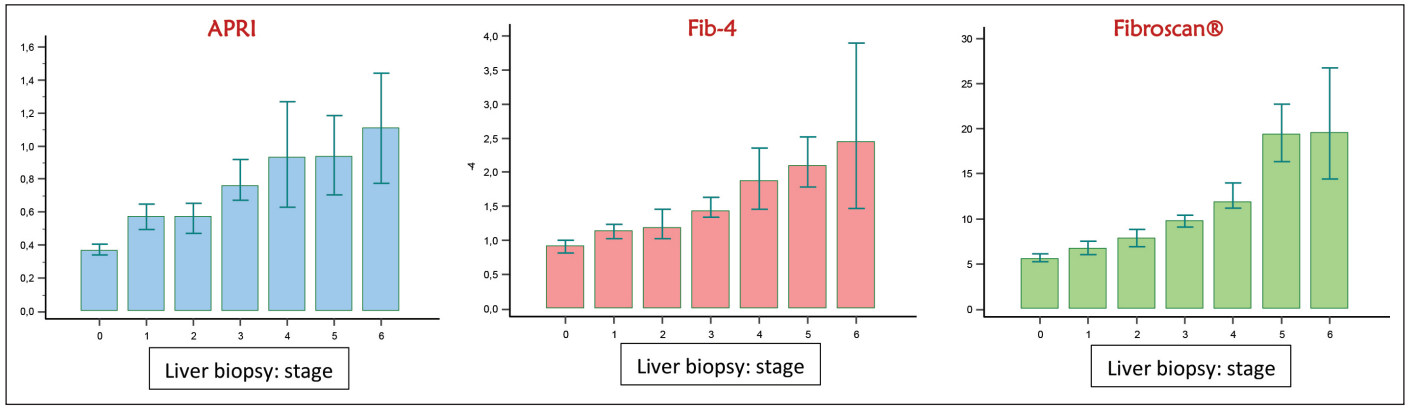

Figure 2. Median (95% CI) values of non-invasive fibrosis indicators at different stages of liver biopsy.

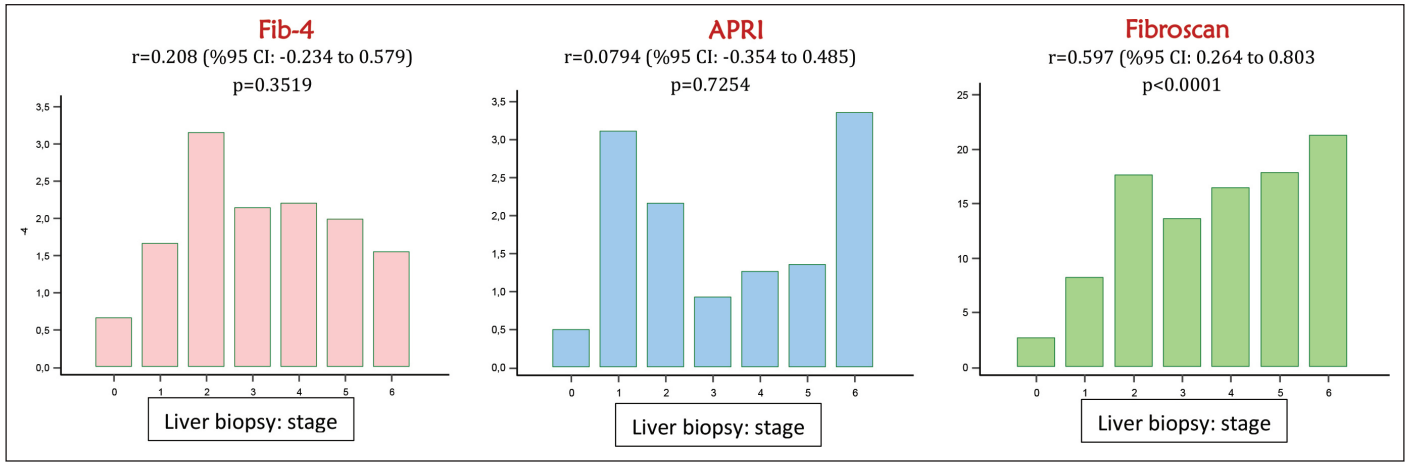

Figure 3. Relationship between stage in liver biopsy and non-invasive indicators in patients with autoimmune hepatitis.

Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021) was used for statistical analysis and graph generation.

Ethical Approval

As stated in the 1964 Declaration of Helsinki and its subsequent amendments, all methods in our study were conducted in accordance with the ethical standards of the national research committee. Ethics committee approval was obtained from Ege University Faculty of Medicine Clinical Research Ethics Committee on March 4, 2021, with decision number 21-3T/62. Written informed consent was obtained from all participating patients.

Results

A total of 1,814 patients underwent liver biopsy between June 2014 and December 2020. After excluding patients with a biopsy date more than 3 months apart from the FS procedure, those lacking sufficient data for APRI and FIB-4 calculations, individuals with ascites, HCC, inadequate biopsy samples, and insufficient FS measurements, a total of 778 patients remained in the study cohort. Of these patients, 417 (53.6%) were female. The mean age was 48.8±13.8 years, and the median age was 51 years. The mean FIB-4 score was 1.837±2.144 (median: 1.247), while the mean APRI score was 1.285±2.866 (median: 0.590). The mean FS measurement was 10.6±9.7 kPa (median 7.9 kPa), while the mean fibrosis score on liver biopsies was 1.87±1.75 (median: 1). All three methods showed strong correlation with histological fibrosis; however, FS demonstrated a statistically significantly superior relationship compared to FIB-4 and APRI. The correlation of non-invasive fibrosis markers with the histological stage of liver fibrosis is presented in Figure 1. In all three methods, as histological stage increases, the measurement values rise in parallel. The correlations of non-invasive fibrosis markers with different fibrosis grades in liver biopsy are presented in Figure 2.

The disease diagnoses, in order of frequency, were HBV (n=228), metabolic dysfunction-associated steatotic liver disease (MASLD) (n=185), HCV (n=58), cryptogenic (n=53), primary biliary cholangitis (n=40), autoimmune hepatitis (AIH) (n=28), overlap syndrome (OS) (n=23), multiple diagnoses (n=42), and other diagnoses (n=83). The relationship between non-invasive fibrosis markers and histological fibrosis in various liver diseases is presented in Table 1. As seen in Table 1, in AIH and OS, FIB-4 and APRI scores do not show a consistent increase correlating with histological stage, whereas FS demonstrates a consistent increase correlating with histological stage. The correlation of different non-invasive tests with the grade of fibrosis obtained on liver biopsy in AIH and OS is presented in Figure 3 and 4. In contrast to these two diseases, in patients with MASLD, all three methods are concordant with histological stage, but FS measurements appear significantly superior compared to the other methods. The relationship between non-invasive markers and liver biopsy stage in MASLD patients (n=185) is presented in Figure 5.

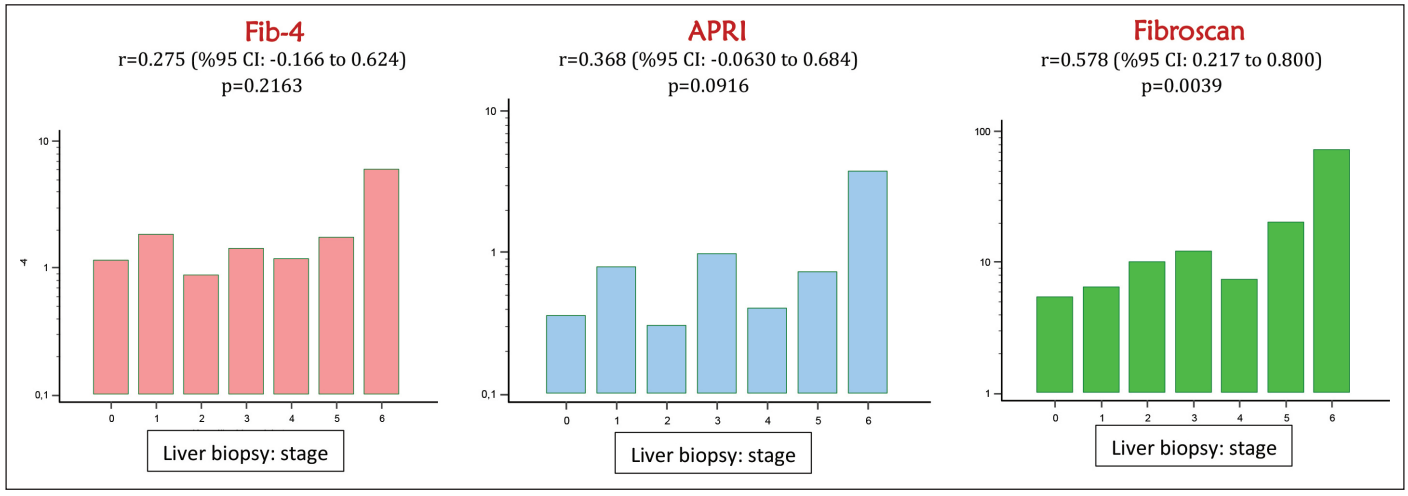

Figure 4. Relationship between stage in liver biopsy and non-invasive indicators in patients with overlap syndrome.

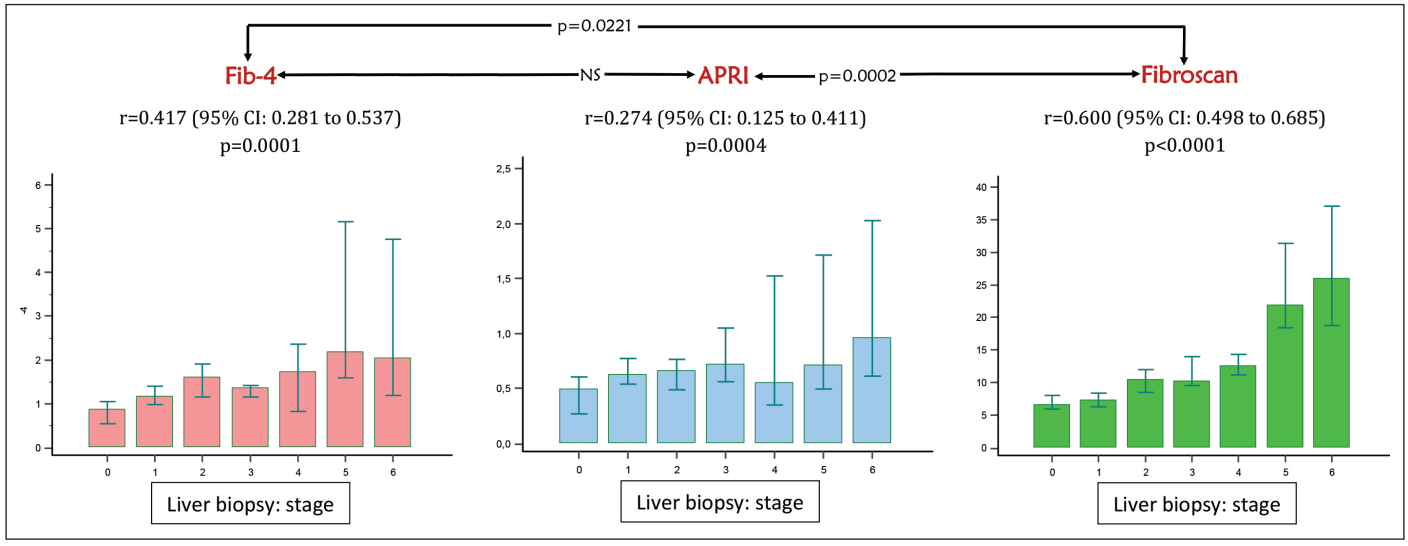

Figure 5. Relationship between stage and non-invasive indicators in liver biopsy in MASLD patients.

Discussion

The degree of fibrosis in the liver is important in predicting liver-related complications independent of the underlying liver disease. The presence of cirrhosis is also associated with clinical decompensation, liver-related mortality, and hepatocellular carcinoma. Therefore, invasive and non-invasive tests are being developed to determine the stages of liver fibrosis. Liver biopsy is still considered the imperfect gold standard. However, due to the ease of repeatability of non-invasive techniques, establishing their correlation with liver biopsy is important.

In the present study, we investigated the correlation of non-invasive techniques (FIB-4, APRI, and FS) with liver biopsy in a cohort of 778 patients. Although all three methods showed strong correlation with histological fibrosis, FS exhibited a statistically significant superior correlation compared to FIB-4 and APRI. Looking at disease-specific data, in patients diagnosed with HBV and HCV, all three non-invasive methods correlated with liver biopsy in detecting significant fibrosis in our study. A study evaluating 520 chronic HBV patients reported that FIB-4 and APRI scores demonstrated similarly good performance compared to FS. Specifically, FIB-4 showed similar performance to APRI in the ≥F2 fibrosis group but outperformed APRI in the F4 fibrosis (cirrhosis) group.[13] The reference diagnostic method in this study was FS.

In another study of 668 chronic HBV patients where liver biopsy was the reference diagnostic method, FIB-4 yielded area under the receiver-operating characteristic curve (AUROC) values of 0.865, 0.910, and 0.926 for detecting ≥F2, ≥F3, and F4 fibrosis, respectively.[14] In a study involving 487 patients diagnosed with HCV, FIB-4 and APRI scores were compared with FS. It was shown that FIB-4 outperformed APRI in detecting advanced fibrosis. Both scores demonstrated good performance in this regard, with FIB-4 having an area under the curve (AUC) of 0.881 (0.850–0.912) and APRI of 0.835 (0.798–0.871) (p<0.0001).[15]

In a correlation study involving 1,029 HCV and 384 HBV patients with known histological fibrosis values determined by liver biopsy, it was found that both APRI and FIB-4 scores increased with advancing histological fibrosis according to the METAVIR grading system in HCV patients. In contrast, among HBV patients, only the FIB-4 score showed an increase with advancing histological fibrosis

Table 1. Association of non-invasive fibrosis markers with histological fibrosis in various liver diseases

		APRI			Fib-4			Transient elastography (FibroScan®)		
Disease	**Patients**	**r**	**95% CI**	**p**	**r**	**95% CI**	**p**	**r**	**95% CI**	**p**
Overall	778	0.372	0.304–0.436	<0.0001	0.403	0.337–0.466	<0.0001	0.553	0.500–0.601	<0.0001
HBV	228	0.436	0.319–0.540	<0.0001	0.346	0.220–0.460	<0.0001	0.505	0.401–0.596	<0.0001
HCV	58	0.555	0.340–0.715	<0.0001	0.621	0.425–0.761	<0.0001	0.647	0.464–0.776	<0.0001
AIH	28	0.0794	-0.354–0.485	0.7254	0.208	-0.234–0.579	0.3519	0.597	0.264–0.803	<0.0001
PBC	40	0.416	0.0905–0.661	0.0144	0.467	0.153–0.696	0.0053	0.493	0.206–0.702	0.0017
Overlap	23	0.368	-0.0630–0.684	0.0916	0.275	-0.166–0.624	0.2163	0.578	0.217–0.800	0.0039
MASLD	185	0.274	0.125–0.411	0.0004	0.417	0.281–0.537	<0.0001	0.6	0.498–0.685	<0.0001
Criptogenic	53	0.421	0.108–0.659	0.0105	0.541	0.258–0.738	0.0007	0.718	0.524–0.841	<0.0001
More than 1	42	0.483	0.193–0.695	0.0021	0.576	0.314–0.756	0.0002	0.539	0.273–0.728	0.0003
Others	83	0.249	0.00376–0.467	0.0469	0.329	0.0890–0.534	0.0084	0.431	0.220–0.604	0.0002

CI: Confidence interval; HBV: Hepatitis B virüs; HCV: Hepatitis C virüs; AIH: Autoimmune hepatitis; PBC: Primary biliary cholangitis; MASLD: Metabolic dysfunction-associated steatotic liver disease.

according to the METAVIR grading system. Additionally, compared to HCV patients, it was shown that the diagnostic accuracy of APRI and FIB-4 for advanced fibrosis and cirrhosis was slightly reduced in HBV patients.[16]

In the present study, it was found that in autoimmune hepatitis and overlap syndrome, the FIB-4 and APRI scores did not show a consistent increase with histological stage; however, FS showed a consistent increase with histological stage. In the evaluation of 100 AIH patients who underwent liver biopsy, FS was found to be more successful than FIB-4 and APRI in detecting ≥F3 fibrosis. The METAVIR scoring system was used for histological evaluation in this study. Unlike in our study, this study found that while the APRI and FIB-4 scoring systems had a lower correlation with histological fibrosis compared to FS, they were still significantly correlated.[17] In the present study, the small number of patients in both the autoimmune hepatitis group and the overlap syndrome group may have led to a Type 2 error.

In our study, all three non-invasive techniques were found to correlate with the level of histological fibrosis in patients with primary biliary cholangitis. Data from 103 patients diagnosed with primary biliary cholangitis who underwent liver biopsy showed that FS had a stronger correlation with the level of histological fibrosis compared to APRI and FIB-4.[18] In the EASL guidelines, a threshold value of 10 kPa for FS is recommended for detecting significant fibrosis, while the routine use of other laboratory-based non-invasive scores for PBC in clinical practice is not advised.[19]

In the present study, all three methods were in agreement with histological stage in MASLD patients, with FS measurements showing notably superior agreement compared to the others. In a meta-analysis of 36 studies involving 9,074 patients, despite the drawbacks of the FIB-4 score, it was reported to have an AUROC of 0.80 and a positive predictive value of >90% for excluding advanced fibrosis in MASLD patients.[20] In the same meta-analysis, the diagnostic accuracy of FS for advanced fibrosis was reported with an AUC of 0.87 for the M probe and 0.86 for the XL probe in the analysis of 2,960 patients.[20] Although FS has a negative predictive value (NPV) above 90% for excluding advanced fibrosis, it generally exhibits a lower positive predictive value (PPV) compared to viral hepatitis and can lead to false positive results in MASLD patients.[21,22] The EASL recommends an 8 kPa threshold as the most validated cutoff value for excluding advanced fibrosis in MASLD patients.[19]

A key strength of the present study is its demonstration of histological correlations between widely used non-invasive methods—FIB-4, APRI scores, and FS—and invasive liver biopsy in a large cohort of 778 patients across different diseases. Despite being retrospective, our study relies on objective data from hospital databases, eliminating concerns related to recall bias.

Limitations of the study include its retrospective design, which could have resulted in incomplete data collection for all patients, and the potential for Type 2 errors due to small sample sizes in specific patient groups (such as autoimmune hepatitis and overlap syndrome).

Conclusion

In conclusion, non-invasive fibrosis markers (FIB-4, APRI, and FS) demonstrate good correlation with histological fibrosis, particularly in MASLD, where evaluation with FS, if available, should be preferred. Laboratory-based indicators should be avoided for assessing fibrosis in patients with autoimmune hepatitis and overlap syndrome.

Ethics Committee Approval: The Ege University FAculty of Medicine Clinical Research Ethics Committee granted approval for this study (date: 04.03.2021, number: 21-3T/62).

Author Contributions: Concept – USA, FG, ND; Design – USA, FG, ND; Supervision – USA, OO, GE, ZK, IT; Fundings – ND, FY, DN; Materials – ND, FY, DN, IT, FG; Data Collection and/or Processing – ND, USA; Analysis and/or Interpretation – ND, USA; Literature Search – ND, USA; Writing – ND, USA; Critical Reviews – USA, OO, GE, ZK, IT, FG, ND.

Conflict of Interest: The authors have no conflict of interest to declare.

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References

1. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy. Hepatology. 2009;49(3):1017-1044.
2. Alahdab YÖ, Yilmaz Y. Transient Elastografi (FibroScan®): Karaciğer fibrozisini değerlendirmede yeni bir ufuk. Güncel Gastroenteroloji 2013;17(1):59-64. [Turkish]
3. Özbek SS. Karaciğer elastrografisi. Türk Radyoloji Seminerleri 2019;7:13-24.
4. Roulot D, Czernichow S, Le Clésiau H, Costes JL, Vergnaud AC, Beaugrand M. Liver stiffness values in apparently healthy subjects: influence of gender and metabolic syndrome. J Hepatol 2008;48(4):606-613.
5. Fung J, Lai CL, Chan SC, But D, Seto WK, Cheng C, et al. Correlation of liver stiffness and histological features in healthy persons and in patients with occult hepatitis B, chronic active hepatitis B, or hepatitis B cirrhosis. Am J Gastroenterol 2010;105(5):1116-1122.
6. Kim SU, Choi GH, Han WK, Kim BK, Park JY, Kim DY, et al. What are 'true normal' liver stiffness values using FibroScan?: a prospective study in healthy living liver and kidney donors in South Korea. Liver Int 2010;30(2):268-274.
7. Gatos I, Drazinos P, Yarmenitis S, Theotokas I, Zoumpoulis PS. Comparison of sound touch elastography, shear wave elastography and vibration-controlled transient elastography in chronic liver disease assessment using liver biopsy as the "reference standard". Ultrasound Med Biol 2020;46(4):959-971.
8. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; 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(2):370-398.
9. Ziol M, Handra-Luca A, Kettaneh A, Christidis C, Mal F, Kazemi F, et al. Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C. Hepatology 2005;41(1):48-54.
10. 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(3):885-894.
11. Boursier J, Zarski JP, de Ledinghen V, Rousselet MC, Sturm N, Lebail B, et al. Determination of reliability criteria for liver stiffness evaluation by transient elastography. Hepatology 2013;57(3):1182-1191.
12. Ishak K, Baptista A, Bianchi L, Callea F, De Groote J, Gudat F, et al. Histological grading and staging of chronic hepatitis. J Hepatol 1995;22(6):696-699.
13. Rungta S, Kumari S, Verma K, Akhtar G, Deep A, Sr., Swaroop S. A comparative analysis of the apri, fib4, and fibroscan score in evaluating the severity of chronic liver disease in chronic hepatitis B patients in India. Cureus 2021;13(11):e19342.
14. Kim BK, Kim DY, Park JY, Ahn SH, Chon CY, Kim JK, et al. Validation of FIB-4 and comparison with other simple noninvasive indices for predicting liver fibrosis and cirrhosis in hepatitis B virus-infected patients. Liver Int 2010;30(4):546-553.
15. Rungta S, Kumari S, Deep A, Verma K, Swaroop S. APRI and FIB-4 performance to assess liver fibrosis against predefined Fibroscan values in chronic hepatitis C virus infection. J Family Med Prim Care 2021;10(11):4082-4088.
16. Itakura J, Kurosaki M, Setoyama H, Simakami T, Oza N, Korenaga M, et al. Applicability of APRI and FIB-4 as a transition indicator of liver fibrosis in patients with chronic viral hepatitis. J Gastroenterol 2021;56(5):470-478.
17. Xu Q, Sheng L, Bao H, Chen X, Guo C, Li H, et al. Evaluation of transient elastography in assessing liver fibrosis in patients with autoimmune hepatitis. J Gastroenterol Hepatol 2017;32(3):639-644.
18. Corpechot C, Carrat F, Poujol-Robert A, Gaouar F, Wendum D, Chazouillères O, et al. Noninvasive elastography-based assessment of liver fibrosis progression and prognosis in primary biliary cirrhosis. Hepatology 2012;56(1):198-208.
19. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; Clinical Practice Guideline Panel; Chair:; EASL Governing Board representative:; Panel members:. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. J Hepatol 2021;75(3):659-689.
20. Xiao G, Zhu S, Xiao X, Yan L, Yang J, Wu G. Comparison of laboratory tests, ultrasound, or magnetic resonance elastography to detect fibrosis in patients with nonalcoholic fatty liver disease: A meta-analysis. Hepatology 2017;66(5):1486-1501.
21. Eddowes PJ, Sasso M, Allison M, Tsochatzis E, Anstee QM, Sheridan D, et al. Accuracy of fibroscan controlled attenuation parameter and liver stiffness measurement in assessing steatosis and fibrosis in patients with nonalcoholic fatty liver disease. Gastroenterology 2019;156(6):1717-1730.
22. Vuppalanchi R, Siddiqui MS, Van Natta ML, Hallinan E, Brandman D, Kowdley K, et al. Performance characteristics of vibration-controlled transient elastography for evaluation of nonalcoholic fatty liver disease. Hepatology 2018;67(1):134-144.