

Comparison of Non-Alcoholic Fatty Liver Disease Fibrosis Score and Fibrosis-4 Index with Transient Elastography Results in the Evaluation of Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease

Parinaz Shariati¹, Elham Mokhtari Amirmajdi^{2*}, Seyedeh Zahra Mostafavian³

¹General Practitioner, Medical Sciences Branch, Islamic Azad University, Mashhad, Khorasan Razavi, Iran

²Assistant professor, Gastroenterologist and Hepatologist, Department of Internal Medicine, MMS.C., Islamic Azad University, Mashhad, Iran

³Associate professor, Department of Community medicine, MMS.C., Islamic Azad University, Mashhad, Iran

ABSTRACT

Background:

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common condition that can lead to serious liver complications. Transient elastography is a reliable, non-invasive, but expensive method for diagnosing fibrosis. This study compared the performance of non-alcoholic fatty liver disease (NAFLD) fibrosis score and fibrosis-4 (FIB-4) index as cheaper methods, with transient elastography in Mashhad, Iran.

Materials and Methods:

The study included 67 patients with MASLD. Demographic, laboratory, and elastography data were collected. Data were analyzed using SPSS software version 27 with two approaches: first, applying cutoffs from previous studies (NAFLD score > -1.455, elastography \geq 8.7 kPa, FIB-4 > 1.30); second, calculating ROC curves to find optimal cutoffs for each index. P values \leq 0.05 were significant.

Results:

Based on previous cutoffs, the FIB-4 at 1.3 showed sensitivity 45%, specificity 97.8%, positive predictive value (PPV) 90%, and negative predictive value (NPV) 80%. The NAFLD score at -1.455 had a sensitivity of 55%, a specificity of 93.6%, a PPV of 78.5%, and an NPV of 83%. In this study, ROC analysis gave FIB-4 cutoff 1.335 with sensitivity 45%, specificity 100%, PPV 100%, and NPV 81%. The NAFLD score cutoff -1.93 showed sensitivity 75%, specificity 91.5%, PPV 79%, and NPV 89.5%.

Conclusion:

Based on the results, the NAFLD fibrosis score demonstrated better performance in ruling out the disease, while FIB-4 showed superior accuracy in diagnosing fibrosis. However, the combined use of multiple indices may reduce unnecessary referrals and improve the clinical management of patients.

Keywords: Metabolic dysfunction-associated steatotic liver disease, NAFLD fibrosis score, FIB-4 index, Transient elastography, FibroScan

please cite this paper as:

Shariati P, Mokhtari Amirmajdi E. Comparison of Non-Alcoholic Fatty Liver Disease Fibrosis Score and Fibrosis-4 Index with Transient Elastography Results in the Evaluation of Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease. *Govareh*.2026;30: 180-191.

**Corresponding Author:*

Elham Mokhtari Amirmajdi, MD

Address : Aria Hospital, East Chamran street, Mashhad, Iran

Tel:+ 98 5132229095

Fax : + 98 5137603458

Email: emokhtaria@mshiau.ac.ir

Received: 10 Sep. 2025

Revised: 28 Nov. 2025

Accepted: 29 Nov. 2025

INTRODUCTION

Alcoholic fatty liver disease and metabolically associated liver diseases represent the two most common forms of liver disorders, both characterized by cytoplasmic accumulation of triglycerides in hepatic lobules. These conditions may progress to cirrhosis, hepatic failure, hepatocellular carcinoma, and even death (1). In 2023, a joint consensus by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) updated the terminology of non-alcoholic fatty liver disease (NAFLD), renaming it as metabolic dysfunction-associated steatotic liver disease (MASLD) (2). Since approximately 99% of cases previously classified as NAFLD overlap with MASLD, the term MASLD is also used in this study (3). Globally, MASLD affects nearly 30% of the population, a prevalence that is increasing in parallel with rising obesity rates (4). It is currently the leading cause of chronic liver disease, impacting over 38% of adults worldwide and 7-14% of children (4, 5). By 2040, the global prevalence is projected to reach 55.4% (6).

In the Middle East and North Africa (MENA) region, MASLD has been shown to be highly prevalent. In 2020, the estimated prevalence in the general population was 39.43%, while among patients with type 2 diabetes it reached 68.71%. Egypt, Turkey, and Iran are predicted to bear the highest national burdens in this region (7). A major complication of MASLD is cirrhosis, accompanied by a markedly increased risk of cardiovascular events, which together represent the leading causes of mortality in affected patients (8-10).

Therefore, accurate staging of liver fibrosis and early detection are crucial (11). Early identification allows high-risk individuals to benefit from lifestyle modification and timely referral for secondary care, while patients with cirrhosis can undergo early screening for esophageal varices and hepatocellular carcinoma (12).

Although liver biopsy remains the gold standard for diagnosing metabolic dysfunction-associated steatohepatitis (MASH), its invasiveness and associated risks, including mortality, limit its routine use for long-term monitoring of fibrosis progression (13, 14). In response, there is growing interest in reliable, cost-effective, and non-invasive biomarkers to replace biopsy for fibrosis staging in MASLD (12).

Transient elastography has emerged as a widely adopted non-invasive alternative that provides greater accuracy than biopsy in certain clinical settings (15). Additionally, several scoring systems have been developed, including the NAFLD fibrosis score, fibrosis-4 (FIB-4) index, aspartate aminotransferase (AST) to platelet ratio index (APRI),

and various biomarker panels such as the enhanced liver fibrosis (ELF) panel, FibroMeter, FibroTest, and HepaScore (16). The NAFLD fibrosis score incorporates six parameters: age, body mass index (BMI), platelet count, hyperglycemia, serum albumin, and AST/ALT (alanine aminotransferase) ratio (17). The FIB-4 index is calculated from platelet count, ALT, AST, and age (16). Comparative studies have demonstrated that FIB-4 and transient elastography outperform other indices in predicting fibrosis when validated against biopsy (18). Despite extensive international research (11, 12, 14, 19–23), there is limited evidence from Iran. Accordingly, the present study aimed to evaluate the diagnostic performance of the NAFLD fibrosis score and FIB-4 index in comparison with transient elastography among Iranian patients with MASLD.

MATERIALS AND METHODS

Between 2022 and 2024, a cross-sectional study was conducted among patients with MASLD attending internal medicine clinics at hospitals affiliated with the Islamic Azad University of Mashhad. Diagnosis was established by a gastroenterologist using a combination of clinical assessment, patient history, laboratory parameters, and ultrasound findings, in line with EASL and EASD recommendations. Only patients who met the inclusion criteria and provided written informed consent were considered eligible. Baseline characteristics, including age, sex, BMI, smoking and alcohol habits, diabetic status, and lipid profile, were documented for each participant. All individuals underwent transient elastography (FibroScan), through which both the stage of liver fibrosis and the controlled attenuation parameter (CAP), an indicator of hepatic fat accumulation, were obtained.

For confidentiality, each participant was assigned a specific code, and data were securely managed in an Excel database. The target sample size was guided by the work of Ben Cox and others (19), which reported that with a FibroScan cutoff of ≥ 8.7 kPa, the FIB-4 score demonstrated a sensitivity of 53.1% (95% CI; $d = p/4$). Based on this calculation, the minimum required sample size was 55 patients. Nevertheless, in this study, all eligible individuals presenting during the 2-year enrollment period were included, resulting in a larger sample than the estimated minimum.

$$N = z_{1-\alpha/2} p(1-p) / d^2 = 1.96^2 \cdot 0.513(1-0.513) / 0.1282^2 = 55$$

Study inclusion criteria: Age over 18 years and a definitive diagnosis of MASLD by a gastroenterologist

Study exclusion criteria: Incomplete information, other chronic liver diseases (hepatitis B and C, autoimmune

diseases, cirrhosis, use of hepatotoxic drugs (such as methotrexate), congestive heart failure, alcohol consumption, use of hormonal or herbal drugs, BMI > 35 kg/m², limitations in performing FibroScan

Elastography results for non-alcoholic fatty liver were classified and recorded as follows:

• F0: 1–6 kPa_ F1: 6.1–7 kPa_ F2: 7.1–9 kPa_ F3: 9.1–17 kPa_ F4: ≥ 17 kPa

The parameter score (CAP), which indicates the extent of fatty liver change, was also determined and recorded on elastography for each patient. The following measurements were performed on random blood samples from all patients within 1 month of the FibroScan evaluation (24).

The results of the tests were evaluated as follows:

1) Dyslipidemia was defined as total cholesterol ≥200 mg/dL, or triglycerides ≥150 mg/dL, or low-density lipoprotein-cholesterol (LDL-C) ≥130 mg/dL, or high-density lipoprotein-cholesterol (HDL-C) <40 mg/dL (for men) and <50 mg/dL (for women) (25-27).

2) Serum ALT with a value of about 45 U/L as the upper limit of normal in men and about 30 in women, serum AST with a value of 15-37 U/L as the normal range, platelet count with 150,000-400,000/μL as the normal range

3) If the patient did not know his diabetes and sugar status: If any of the following were positive and he had symptoms of polyuria and polydipsia, diabetes was considered:

- Random blood sugar: greater than or equal to 200 mg/dL
- Fasting blood sugar: greater than or equal to 126 mg/dL
- Glucose tolerance test(GTT: sugar two hours after consuming 75 grams of glucose): greater than or equal to 200 mg/dL
- HbA1c: greater than or equal to 5.6%

How to calculate the two indices FIB-4 and NAFLD fibrosis score

1) NAFLD fibrosis score: $-1.675 + 0.037 \times \text{age (years)} + 0.094 \times \text{BMI (kg/m}^2) + 1.13 \times \text{impaired fasting glycaemia or diabetes (yes = 1, no = 0)} + 0.99 \times \text{AST/ALT ratio} - 0.013 \times \text{platelet (} \times 10^9/\text{L)} - 0.66 \times \text{albumin (g/dL)}$

2) FIB-4 score = $(\text{age} \times \text{AST}) / (\text{Platelet count} \times (\text{square root of ALT}))$

After performing the tests, two NAFLD and fib-4 scores were calculated using the formulas, and their results were compared with elastography using statistical methods (24).

Data analysis method

In this study, SPSS software version 26 was used to analyze the data. We used mean, standard deviation, frequency, and percentage to describe the results. In order to achieve better results, we used two methods for data analysis:

1) Calculation of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), using the cutoff point of previous studies as -1.455 for the NAFLD score, ≥8.7 for FibroScan, and >1.3 for the FIB-4 index (19).

2) Drawing receiver operating characteristic (ROC) curves to determine the diagnostic value of FIB-4 and NAFLD score, and calculating the area under the ROC curve (AUROC) for each non-invasive index to differentiate F1 and F2 liver fibrosis from F3 and F4 with a cutoff of 8.7, and determining the optimal cutoff of both indices using ROC curves. And calculating the Youden index, then sensitivity, specificity, PPV, and NPV were also calculated for these cutoffs, and P ≤ 0.05 values were considered statistically significant (24).

To identify factors associated with the discrepancy between non-invasive indices and FibroScan, multivariate logistic regression was used. In this analysis, variables such as age, sex, BMI, diabetes, hyperlipidemia, smoking, and alcohol consumption, biochemical indices ALT, AST, albumin, HbA1c, and FBS were entered into the model. A significance level of less than 0.05 was considered statistically significant. In addition, odds ratio (OR) values were reported with 95% confidence intervals to interpret the strength of the association. The number 1 was considered for agreement and 0 for disagreement.

RESULTS

Patient demographic information

This cross-sectional investigation aimed to evaluate the correlation between the NAFLD fibrosis score and FIB-4 index with transient elastography findings for liver fibrosis assessment. A total of 83 patients were initially considered, and after applying the exclusion criteria, 67 individuals with NAFLD were enrolled. Among them, 38 patients (56.7%) were women, and 29 (43.3%) were men. The participants had a mean age of 44.08 years (SD = 11.26) and a mean BMI of 29.57 kg/m² (SD = 4.08).

Current smokers accounted for 7.5% of the cohort, while 32.8% had a history of smoking. Occasional alcohol consumption in the past, not sufficient to classify as alcoholic fatty liver, was reported by 16.4% of patients. Additionally, 14.9% had diabetes, and 26.9% were diagnosed with hyperlipidemia (Table 1).

Table 1. Distribution of demographic findings in the study population

Section	Variable	Category	Minimum	Maximum	Mean	SD	Frequency	Percent
Quantitative demographic data	Age (years)	–	24	67	44.08	11.26	–	–
	Height (cm)	–	147	192	168.89	10.83	–	–
	Weight (kg)	–	50	127	84.50	14.55	–	–
	BMI (kg/m ²)	–	21.36	44.43	29.57	4.08	–	–
Qualitative demographic data	Smoking	Never	–	–	–	–	40	59.7
		Past	–	–	–	–	22	32.8
		Current	–	–	–	–	5	7.5
		Total	–	–	–	–	67	100
	Alcohol	Never	–	–	–	–	56	83.6
		Past	–	–	–	–	11	16.4
		Total	–	–	–	–	67	100
	Diabetes	No	–	–	–	–	57	85.1
		Yes	–	–	–	–	10	14.9
		Total	–	–	–	–	67	100
	Hyperlipidemia	No	–	–	–	–	49	73.1
		Yes	–	–	–	–	18	26.9
Total		–	–	–	–	67	100	

BMI: body mass index

Results of laboratory tests and indices of elastography are summarized in table 2 and table-3.

Table 2. Distribution of laboratory findings in the study population

Variable	Minimum	Maximum	Mean	Standard Deviation
ALT (U/L)	12	154	37.31	24.79
AST (U/L)	11	141	32.89	19.96
ALP (U/L)	40	432	175.62	69.46
Total Bilirubin (mg/dL)	0.4	2.3	0.83	0.33
Direct Bilirubin (mg/dL)	0.1	1.2	0.24	0.19
Albumin (g/dL)	3.2	5.1	4.1	0.46
Platelet (×10 ⁹ /L)	166	431	285	59
Fasting blood sugar (mg/dL)	79	174	103.3	19.12
HbA1c (%)	4.2	8.2	6.5	0.86
LDL (mg/dL)	42	202	102.9	30.94
Total cholesterol (mg/dL)	82	429	191.82	59.29

ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, LDL: low-density lipoprotein

Table 3. Distribution of liver indices in the study population

Variable	Minimum	Maximum	Mean	Standard Deviation
CAP score	100	400	326.28	51.49
kPa	1.0	22.8	7.33	2.86
NAFLD fibrosis score	-4.7	-0.43	-2.56	1.01
FIB-4	0.27	1.94	0.85	0.38

CAP: controlled attenuation parameter, NAFLD: non-alcoholic fatty liver disease, FIB-4: fibrosis-4

Calculation results based on the cutoff point of previous studies

The results of calculating the sensitivity, specificity, PPV, and NPV of the FIB4 index based on the cutoff point of 1/3 in previous studies based on the gold standard are 45%, 97.5%, 81.8%, and 80%, respectively (Table 4). In other words, given the high false-negative and low false-positive rates, the FIB-4 index, with high predictive value and specificity, performs well for confirming fibrosis. However, because it has low sensitivity, some affected patients may have a negative test in the initial screening.

Table 4. Calculation of sensitivity, specificity, PPV, and NPV of the FIB4 index based on the cutoff point in previous studies based on the gold standard

	Gold standard positive	Gold standard negative	Total
FIB-4 positive	9	2	11
FIB-4 negative	11	45	56
Total	20	47	67

PPV: positive predictive value, NPV: negative predictive value, FIB-4: fibrosis-4

The calculation of sensitivity, specificity, PPV, and NPV of the NAFLD index based on the cutoff point -1.455 in previous studies based on the gold standard was as follows: 55% Sen, 93.6% Spe, 78.5% PPV, 83% NPV (Table 5). In other words, the NAFLD index at the cutoff point of -1.455 had a higher sensitivity and NPV than FIB-4 at the cutoff point of 1.3. At this cutoff point, the NAFLD index performs better at ruling out the disease, but its low sensitivity means that a number of patients may still be falsely reported as negative.

Table 5. Sensitivity, specificity, PPV, and NPV of NAFLD index based on the cutoff point in previous studies based on the gold standard

	Gold standard positive	Gold standard negative	Total
NAFLD positive	11	3	14
NAFLD negative	9	44	53
Total	20	47	67

PPV: positive predictive value, NPV: negative predictive value, NAFLD: non-alcoholic fatty liver disease

Calculation results based on the receiver operating characteristic curve (ROC test). In another method for examining the two FIB-4 and NAFLD indices, the ROC curve was used to determine the area under the curve and the cut points. The ROC curves for the two FIB-4 and NAFLD indices were plotted (Figure 1).

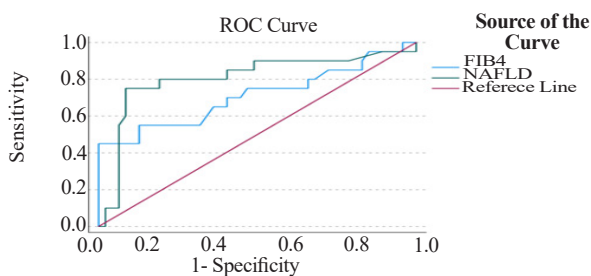


Figure 1. ROC chart of the two FIB-4 and NAFLD indices

The areas under the ROC curves for the two FIB-4 and NAFLD indices were calculated. For the FIB-4 index, the area under the ROC curve was 0.806, the standard error was 0.068, the lower bound was 0.673, the upper bound was 0.940, the probability value was >0.0001, and for the NAFLD index, the area under the ROC curve was 0.711, the standard error was 0.079, the lower bound was 0.557, the upper bound was 0.865, the probability value was 0.007. The area under the curve of both indices is above 50% and is statistically significant (Table 6). The area under the ROC curve for the FIB-4 index is higher; in other words, the FIB-4 index performs better at diagnosing fibrosis.

Table 6. Area under the ROC curve of the two indices FIB-4 and NAFLD

Index	Level	Standard error	Lower bound	Upper bound	P value
FIB-4	0.806	0.068	0.673	0.940	<0.001
NAFLD	0.711	0.079	0.557	0.865	0.007

NAFLD: non-alcoholic fatty liver disease, FIB-4: fibrosis-4

The result of calculating the sensitivity, specificity, PPV and NPV of the FIB-4 index based on the Youden index = 0.45 and at the cutoff point of 1.335 points in the present study based on the gold standard as 45% Sen, 100% Spe, 100% PPV, 81% NPV (Table 7). In other words, at this cutoff point, FIB-4 performs well at confirming the disease.

Table 7. Calculation of the sensitivity, specificity, PPV, and NPV of the FIB-4 index based on the cutoff point in the present study, based on the gold standard

	Gold standard positive	Gold standard negative	Total
FIB-4 positive	9	0	9
FIB-4 negative	11	47	58
Total	20	47	67

PPV: positive predictive value, NPV: negative predictive value, FIB-4: fibrosis-4

Sensitivity, specificity, PPV, and NPV of the NAFLD index, based on the Youden index (0.665) and the cutoff point of -1.93, were calculated in the present study as 75% Sen, 91.5% Spe, 79% PPV, and 89.5% NPV (Table 8).

Table 8. Calculation of sensitivity, specificity, PPV, and NPV of NAFLD index based on the cutoff point in the present study, based on the gold standard

	Gold standard positive	Gold standard negative	Total
NAFLD positive	15	4	19
NAFLD negative	5	43	48
Total	20	47	67

PPV: positive predictive value, NPV: negative predictive value, NAFLD: non-alcoholic fatty liver disease

Evaluation of cases with discrepant FIB-4 and NAFLD fibrosis score results using transient elastography .

Another investigation that was conducted in this study, in addition to the main objectives, was to calculate the cases of inconsistency between the results of the two NAFLD scores and FIB-4 with the results of transient elastography. The effect of different variables on this concordance and inconsistency was reported in Tables 9-12.

According to Tables 4 and 10, in the investigation of cases of inconsistency between NAFLD score results and elastography at both cutoff points, the percentage of inconsistency at the cutoff point of -1.455 was slightly higher than that at the cutoff point of -1.93 (16.4% versus 13.4%), and at both cutoff points more than 80% of the samples were in agreement.

Table 9. Disagreement between NAFLD score (-1.93) and elastography (8.7)

Frequency (%)	Frequency	Status
13.4%	9	Non-concordant
86.6%	58	Concordant

NAFLD: non-alcoholic fatty liver disease

Table 10. Disagreement between NAFLD Score (-1.455) and elastography (8.7%)

Frequency (%)	Frequency	Status
16.4%	11	Non-concordant
83.6%	56	Concordant

NAFLD: non-alcoholic fatty liver disease

Table 13. Results of logistic regression model of the effect of variables on mismatch for NAFLD score at cutoff point -1.93 and elastography (8.7)

Variable	B	Standard Error (S.E.)	Wald	df	Sig.	Odds Ratio (OR = Exp(B))	95% CI for OR
Age	0.095	0.090	1.119	1	0.290	1.10	0.92 – 1.31
Sex (Ref = Female)	3.353	2.585	1.683	1	0.195	28.58	0.18 – 4530.25
Smoking	-2.712	1.448	3.508	1	0.061	0.066	0.004 – 1.134
Alcohol	-1.750	2.368	0.546	1	0.460	0.174	0.000 – 253.018
BMI	0.120	0.110	1.190	1	0.275	1.13	0.91 – 1.40
Diabetes	-10.974	4.927	4.961	1	0.026	0.000	0.000 – 0.268
Hyperlipidemia	-2.351	1.893	1.543	1	0.214	0.095	0.002 – 3.89
ALT (IU/L)	-0.182	0.145	1.572	1	0.210	0.833	0.627 – 1.108
AST (IU/L)	0.310	0.237	1.717	1	0.190	1.364	0.857 – 2.169
Platelet (10 ⁹ /L)	-0.001	0.007	0.021	1	0.886	0.999	0.986 – 1.012
Albumin (g/L)	1.456	1.819	0.641	1	0.423	4.29	0.12 – 151.69
FBS (mg/dL)	0.346	0.188	3.411	1	0.065	1.41	0.98 – 2.04
HbA1c (%)	-3.605	2.168	2.765	1	0.096	0.027	0.000 – 1.90
Constant	-19.588	24.044	0.664	—	0.415	0.000	—

*P<0.05 is considered significant. BMI: body mass index, FBS: fasting blood sugar, NAFLD: non-alcoholic fatty liver disease, ALT: alanine aminotransferase, AST: aspartate aminotransferase

According to Tables 10 and 11, in examining the cases of inconsistency of FIB-4 results with elastography, at both cut points, the percentage of inconsistency at the cut point was 1.3, 19.4% and relative to the cut point was slightly higher at 1.335, 16.4%. The percentage of agreement in both cases was above 80%. This shows that a small change in the cut point can affect the prediction accuracy.

Table 11. Mismatch of FIB-4 index (1.335) and elastography (8.7)

Frequency	Frequency (%)	Status
11	16.4%	Non-concordant
56	83.6%	Concordant

FIB-4: fibrosis-4

Table 12. Mismatch of FIB-4 index (1.3) and elastography (8.7)

Frequency (%)	Frequency	Status
19.4%	13	Non-concordant
80.5%	54	Concordant

FIB-4: fibrosis-4

Overall, both the NAFLD score and FIB-4 index had greater than 80% agreement with elastography, and a small change in the cutoff number caused a slight change in the discrepancy. These findings suggest that both tools can be useful as predictors of liver fibrosis. However, the precise choice of the cutoff point for each index is important.

According to the study in Table 13, diabetes was a significant variable (P=0.026) and was associated with a significant decrease in the likelihood of matching. Smoking, FBS, and HbA1c are close to significant. And probably have an important clinical effect. Other variables,

including PLT, age, sex, BMI, and liver enzymes, did not show a significant relationship (P>0.05). The model had the highest power in correctly identifying matching cases (98.3%) and had an average performance in identifying mismatches (66.7%).

Table 14. Results of the logistic regression model of the effect of variables on mismatch for NAFLD score at the cutoff point of -1.455

Variable	Coefficient (B)	Standard Error (S.E.)	Wald Statistic	df	Significance (Sig.)	Odds Ratio (OR = Exp(B))	95% CI for OR
Age (years)	0.208	0.143	2.119	1	0.145	1.231	0.931 – 1.628
Sex (Ref = Female)	-1.813	3.578	0.257	1	0.612	0.163	0.000 – 181.346
Smoking	0.976	2.655	3.508	1	0.061	2.653	0.015 – 483.020
Alcohol consumption	-1.513	3.595	0.177	1	0.674	0.220	0.000 – 253.018
BMI	0.350	0.180	3.750	1	0.053	1.41	0.995 – 2.398
Hyperlipidemia	6.854	5.395	1.614	1	0.204	947.771	0.024 – 37,046,106.011
Diabetes	-15.577	8.531	3.334	1	0.068	0.000	0.000 – 3.139
ALT (IU/L)	-0.182	0.145	1.572	1	0.210	0.833	0.627 – 1.108
AST (IU/L)	0.310	0.237	1.717	1	0.190	1.364	0.857 – 2.169
Albumin (g/L)	7.022	4.573	2.358	1	0.125	1121.138	0.144 – 8,747,217.707
FBS (mg/dL)	0.435	0.224	3.750	1	0.053	1.545	0.995 – 2.398
HbA1c (%)	-4.134	3.239	1.630	1	0.202	0.016	0.000 – 9.146
Platelet (10 ⁹ /L)	0.028	0.028	1.052	1	0.305	1.029	0.975 – 1.086
Constant	-50.231	46.779	1.153	1	0.283	0.000	—

BMI: body mass index, FBS: fasting blood sugar, NAFLD: non-alcoholic fatty liver disease, ALT: alanine aminotransferase, AST: aspartate aminotransferase

In the calculations in Table 14, the logistic regression model with a cutoff of 0.500 correctly classified 91% of all cases. The percentage of prediction accuracy was very high in the matching group (96.4%) and in the mismatch group (63.6%). Among the variables entered into the model, none showed a statistically significant relationship; BMI (P = 0.053), FBS (P = 0.053), and diabetes (P = 0.068) were close to significance. Each mg/dL increase in FBS

was associated with an approximately 54% increase in the odds of matching (OR = 1.545), while having diabetes was associated with a significant decrease in the odds of matching to almost zero. Other variables, including age, sex, smoking, alcohol consumption, hyperlipidaemia, ALT, AST, albumin, and PLT, did not show a significant relationship with the outcome.

Table 15. Results of the logistic regression model of the effect of variables on non-compliance for FIB-4 at the cutoff point of 1.335

Variable	B	S.E.	Wald	df	Sig.	OR (Exp(B))	95% CI for OR
Age (years)	-0.083	0.074	1.240	1	0.265	0.921	0.796 – 1.065
Sex (ref = Female)	-1.649	1.936	0.726	1	0.394	0.192	0.004 – 8.541
Smoking	-0.716	1.151	0.387	1	0.534	0.488	0.051 – 4.664
Alcohol consumption	-1.156	2.192	0.278	1	0.598	0.315	0.004 – 23.121
BMI	0.105	0.075	1.967	1	0.161	1.110	0.959 – 1.285
Diabetes	-2.490	1.903	1.711	1	0.191	0.083	0.002 – 3.457
Hyperlipidemia	-0.234	1.321	0.031	1	0.859	0.791	0.059 – 10.532
ALT (IU/L)	-0.080	0.050	2.551	1	0.110	0.923	0.837 – 1.018

Table 15. Results of the logistic regression model of the effect of variables on non-compliance for FIB-4 at the cutoff point of 1.335

Variable	B	S.E.	Wald	df	Sig.	OR (Exp(B))	95% CI for OR
AST (IU/L)	0.101	0.064	2.459	1	0.117	1.106	0.975 – 1.255
Albumin (g/L)	-0.214	1.577	0.018	1	0.892	0.808	0.037 – 17.751
FBS (mg/dL)	0.105	0.075	1.967	1	0.161	1.110	0.959 – 1.285
HbA1C (%)	-2.471	1.764	1.963	1	0.161	0.084	0.003 – 2.679
Platelets (10 ⁹ /L)	0.020	0.025	0.640	1	0.423	1.020	0.971 – 1.072
Constant	16.028	20.938	0.586	1	0.444	91,419,445.915	—

BMI: body mass index, FBS: fasting blood sugar, FIB-4: fibrosis-4, ALT: alanine aminotransferase, AST: aspartate aminotransferase

According to Table 15, the logistic regression model with a cutoff of 0.500 correctly classified 91% of all cases. The prediction accuracy in the very high match group was 98.3%, and in the lower mismatch group, 37.5%. Among the variables entered into the model, none of the variables were significant at the 0.05 level. Although ALT with P=0.110, AST with P=0.11, FBS with P=0.161, HbA1C with P=0.161, and diabetes with P=0.191 had P values close to the threshold of significance and may be clinically

important. The OR estimate showed that each unit increase in AST increased the probability of match occurrence by about 10% (OR=1.106) and each unit increase in ALT decreased the probability by about 7.7% (OR=0.923), although these relationships were not statistically significant. Other variables, including age, sex, smoking, alcohol consumption, hyperlipidemia, and albumin, were not significantly associated with non-compliance at the cutoff point of 1.335.

Table 16. Results of the logistic regression model of the effect of variables on non-compliance for FIB-4 at the cut point of 1.3

Variable	Coefficient (B)	Standard Error (S.E.)	Wald Statistic	df	Significance (Sig.)	Odds Ratio (Exp(B))	95% CI for Exp(B)
Age	-0.359	0.166	4.683	1	*0.030	0.699	0.505 – 0.967
Sex (Ref = Female)	-3.871	2.775	1.946	1	0.163	0.021	0.000 – 4.793
Smoking	-3.905	1.939	4.055	1	*0.044	0.020	0.000 – 0.901
Alcohol Consumption	-1.595	3.551	0.202	1	0.653	0.203	0.000 – 213.564
BMI	0.105	0.075	1.967	1	0.161	1.110	0.959 – 1.285
Hyperlipidemia	10.283	5.276	3.799	1	0.051	29,231.854	0.944 – 9.0×10 ⁸
Diabetes	0.070	2.701	0.001	1	0.979	1.073	0.005 – 213.538
ALT (IU/L)	-0.204	0.108	3.540	1	0.060	0.815	0.659 – 1.009
AST (IU/L)	0.214	0.123	3.016	1	0.082	1.239	0.973 – 1.578
Albumin (g/L)	-4.083	2.696	2.294	1	0.130	0.017	0.000 – 3.323
HbA1c (%)	-5.392	3.043	3.139	1	0.076	0.005	0.000 – 1.773
FBS (mg/dL)	0.105	0.092	1.127	1	0.288	1.102	0.921 – 1.319
Platelet (10 ⁹ /L)	0.020	0.025	0.640	1	0.423	1.020	0.971 – 1.072
Constant	8.551	21.710	0.155	1	0.694	5174.200	—

*P<0.05 is considered significant. BMI: body mass index, FBS: fasting blood sugar, FIB-4: fibrosis-4, ALT: alanine aminotransferase, AST: aspartate aminotransferase

According to Table 16, the logistic regression model was able to predict the status of compliance and non-compliance with an overall accuracy of 95.5%. The model's sensitivity for detecting non-compliance was 81.8%, and its specificity for detecting compliance was 98.2%. In examining the

variables entered into the model, the results showed that age (P=0.030, OR=0.699) and smoking (P=0.036, OR=0.933) had a significant effect on compliance, such that with increasing age and smoking, compliance decreased. Other variables, including hyperlipidemia, ALT, AST, and

HbA1C, although at the borderline of significance, did not show a statistically significant relationship at the 0.05 level. Other factors examined, including sex, alcohol, diabetes, albumin, and FBS, did not have a significant relationship with predicting compliance/non-compliance. In general, based on the results, diabetes was one of the most important factors predicting non-compliance. Also, older age and smoking increase the likelihood of a mismatch. At cutoffs of 1.455 for NAFLD Score and FIB-4 at a cutoff of 1.3, the specified variables had less confounding effect. A slight change in the cutoff point of the indicators can change the prediction accuracy. The best model accuracy was achieved with FIB-4, with a cutoff point of 1.3 (95.5%, sensitivity 81.8%, specificity 98.2%).

DISCUSSION

This study aimed to evaluate the effectiveness of the NAFLD score and the FIB-4 index in comparison with transient elastography (FibroScan) for assessing liver fibrosis in patients with NAFLD. The mean age of participants was 44.08 years, with a standard deviation of ± 11.26 years. Analysis of FIB-4 indicated that it performs very well at correctly identifying individuals without fibrosis, with a sensitivity of 45% and an exceptionally high specificity of 97.5% to 100%. Its PPV ranged between 81.8% and 100%, suggesting that FIB-4 is particularly reliable for confirming fibrosis (rule-in) and guiding further diagnostic investigations, despite its relatively modest sensitivity. In comparison, the NAFLD score, which demonstrated a higher sensitivity of 55% but slightly lower specificity of 93.6%, captured a larger proportion of patients, though the chance of misclassifying healthy individuals increased slightly. Using a cutoff value of -1.93, the NAFLD score maintained relatively high specificity (91.5%), sensitivity (75%), and NPV (89.5%), surpassing FIB-4 (NPV = 81%) and establishing its superiority as a tool for ruling out fibrosis (rule-out). Hannes Hagström and colleagues reported that this score can be used to screen patients at higher risk of developing advanced liver disease by repeated FIB-4 measurements in the clinical setting. The threshold values used to differentiate risk groups in their study were: less than 1.30 for low risk, 1.30 to 2.6 for intermediate risk, and greater than 2.67 for high-risk patients (28). In a study conducted by Cox and others comparing the results of NAFLD fibrosis score (NFS) and FIB-4 scores with transient elastography, NFS had an NPV of 94.1% and FIB-4 had an NPV of 91.6%, and the PPV results were reported as NFS, 32.4%, and FIB-4, 37% (19). The results of this study for NPV were in line with our study. According to their study, these two scores, due to their high NPV, can be helpful in screening patients who

really need transient elastography. However, due to the lower PPV, they have little power in detecting the extent of fibrosis compared with transient elastography (19). Also, in the study by Amernia and co-workers, the FIB-4 score based on the ROC curve showed a sensitivity of 97.7, specificity of 72.7, PPV of 49.4, NPV of 99.2, and accuracy of 78% (24). According to the calculations we performed and the sensitivity of 45%, specificity of 100%, PPV of 100%, and NPV of 81% for the FIB-4 index, the specificity and NPV are almost in line with their study, and the high sensitivity and low PPV in this study are contrary to the research. Other studies have reported that simple fibrosis scores, such as the FIB-4 index, are very suitable as an initial assessment in primary care settings to rule out advanced fibrosis and the risk of future liver-related complications (29). Today, identifying patients with MASLD who develop advanced fibrosis is an important issue for clinicians, and type 2 diabetes, age, and obesity are known risk factors for the development and progression of MASLD (30, 31). The results of the Fib-4 score and transient elastography seem closer together in people over 65 years of age, and age has a less confounding effect at cutoffs of 1.3 and 2 for the Fib-4 score (23). In our study, in cases where the FIB-4 score did not match transient elastography at the cutoff of 1.3, increasing age significantly decreased the likelihood of matching ($P = 0.030$; $OR = 0.699$). Calculation of the accuracy of NFS and FIB-4 compared with FibroScan in a population of 5129 people showed that these two scores had a high false negative and false positive rate in screening patients with NAFLD and were not favorable in patients with various risk factors for NAFLD, and this study introduced waist circumference as the first step in suggesting referral for transient elastography (32). One study reported that the NAFLD fibrosis score was higher in women than in men (AUCs: 0.83 [95% CI: 0.68–0.99] vs. 0.59 [0.46–0.72]; $P=0.016$) (33). However, in our study, sex did not significantly affect the difference between the index results and the elastography results. The performance of non-invasive tests for detecting liver fibrosis in individuals at high risk of MASLD has not been rigorously evaluated. Some studies have shown that these non-invasive tests do not perform well in detecting fibrosis in obese (34) and diabetic patients (35). A cohort study of overweight/obese and diabetic patients also reported poor performance of NFS for significant and advanced fibrosis (36). A comparison of the performance of the FIB-4 and NAFLD score in patients with NAFLD with a BMI of less than 23 and those with a BMI of more than 23 showed that the sensitivity and specificity of the FIB-4 score were not affected by BMI, but the sensitivity of the NFS was affected by BMI and was unacceptably low, to the point that one out

of every two patients with advanced fibrosis might not be diagnosed. Therefore, the NFS should not be used as a first-stage screening tool in lean patients with fatty liver, and FIB-4 is a better screening parameter for advanced NAFLD fibrosis in lean patients (37). A systematic review conducted by Rio in 2021 on the topic of examining the FIB-4, NAFLD score, and APRI showed that all three indices had good performance for predicting hepatic events, with AUC between 0.69 and 0.92. Regarding mortality, this study found that FIB-4 and NFS were much more reliable than APRI. It emphasized that the accuracy of these indices may be affected by factors such as age, platelet count, liver enzyme levels (AST, ALT), and comorbidities (diabetes, hypertension, heart disease) (38). In a study, Chen and colleagues investigated why FIB-4 or NFS results were inconsistent with biopsy in some patients. They reported that among patients with mild fibrosis (F0–F2) whose FIB-4 was higher than 2.67, 13.3% had a history of smoking. In cases where NFS was higher than 0.676 but fibrosis was mild, 20% of patients were smokers. In cases where FIB-4 or NFS was below the threshold but had moderate-to-advanced fibrosis, the percentage of smokers was much lower (e.g., FIB-4 <1.3 in moderate fibrosis, only 3.92% were smokers (39). In our study, diabetes was one of the most important predictors of non-compliance. Also, older age and smoking increased the likelihood of non-compliance at some cutoff points, especially the cutoff point of 1.3. Diagnostic performance of FIB-4 and NAFLD scores and other indices, including APRI, aspartate aminotransferase-to-alanine aminotransferase ratio (AAR), aspartate aminotransferase-to-platelet number index (AP index), fibrosis index (FI), Frons index, BARD score (B: BMI (Body Mass Index) A: Age R: Resistin (a protein associated with inflammation) D: Diabetes (specifically Type 2 diabetes), BAAT score (B: BMI, A: Age, A: Aspartate Aminotransferase (AST), level, T: Total Bilirubin level), and Enhanced Liver Fibrosis test (ELF) have been compared in several studies (20–22). The NPV in a study for the detection of advanced fibrosis was 93%, 91% and 91% for FIB-4, APRI, and NFS, respectively, indicating their utility in ruling out advanced fibrosis (40). Laboratory-based biomarkers (NFS, FIB-4, ELF, or FibroTest) have been reported to be useful tools for the initial assessment of fibrosis (40). According to a review, the most commonly used non-invasive tests for liver fibrosis have excellent NPVs for definitively ruling out advanced fibrosis but yield high false-positive rates, limiting their ability to confirm the diagnosis (41). Several studies have shown that combining non-invasive tests together increases the PPV (36, 42). As a result, various studies have shown that NAFLD score and FIB-4 perform promisingly with high

NPVs. They reduce the need for unnecessary referrals (20, 21). Therefore, low-risk patients can be managed at the primary care level, and fibrosis scores should be calculated periodically (every 1–2 years) to reassess risk (43, 44).

Our study presented several strengths. First, the number of participants exceeded the calculated sample size, and the majority were recruited from a single center, which ensured consistent data collection. Additionally, we employed two methods to evaluate the NFS and FIB-4 scores: one based on cutoff points established in prior studies, and the other based on ROC curve analysis, which allowed for a detailed comparison with transient elastography. However, the study also had limitations. Data collection involved questionnaires alongside laboratory and imaging tests, which may have led some participants to provide incomplete or inaccurate responses. Despite our efforts to gather data promptly, in some cases, obtaining information took over a month. The high cost of transient elastography delayed testing for some patients, and, due to time constraints, these individuals were excluded. The study sample was relatively small and limited to Iranian patients in Mashhad. To achieve more generalizable findings, future research should be multicentric and include patients from various regions of Iran. Standardizing patient characteristics, such as laboratory results and age range, could also enhance the precision of evaluations. In our analysis, we briefly addressed discrepancies between the scores and transient elastography and examined several contributing factors. Investigating the causes of these discrepancies, including patient demographics and laboratory parameters, in larger studies could help determine whether these indices are more applicable to specific patient groups.

The comparison of NAFLD score and FIB-4 with transient elastography demonstrated that both non-invasive indices have substantial diagnostic accuracy in patients with NAFLD. The NAFLD score was more effective in identifying a larger proportion of patients during initial screening (sensitivity 75% vs. 55%) and in ruling out disease by correctly identifying healthy individuals (NPV 89.5% vs. 83%), while FIB-4 showed superior accuracy in confirming fibrosis and guiding referral for additional assessments (PPV 81.8%–100%). The area under the ROC curve was higher for FIB-4 (0.806) compared with NAFLD score (0.711), reflecting its relative advantage in diagnosing fibrosis. Based on these findings and previous research, a combined approach appears beneficial: using the NAFLD score to reliably exclude negative cases initially, followed by FIB-4 evaluation for positive or indeterminate cases. Furthermore, considering relevant risk factors such as smoking and diabetes may enhance patient management and improve clinical outcomes.

ACKNOWLEDGEMENTS:

We would like to thank Dr. Seyedeh Zahra Mostafavian and the internal medicine centers cooperating with Mashhad Azad University.

FINANCIAL SUPPORT:

This study was conducted with the financial support of Islamic Azad University of Mashhad, and, in its design, an attempt was made to examine patients whose tests were in line with their needs and did not impose additional costs.

REFERENCES:

- Lee Goldman M, Andrew I. Schafer, Goldman-Cecil Medicine, Chapter 143. 26 ed 2020.
- 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. *Hepatology*. 2023;78(6):1966-86.
- Mondal T, Smith CI, Loffredo CA, Quartey R, Moses G, Howell CD, et al. Transcriptomics of MASLD pathobiology in African American patients in the Washington DC area. *Int J Molecul. Sci*. 2023;24(23):16654.
- Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology*. 2023;77(4):1335-47.
- Paik JM, Kabbara K, Eberly KE, Younossi Y, Henry L, Younossi ZM. Global burden of NAFLD and chronic liver disease among adolescents and young adults. *Hepatology*. 2022;75(5):1204-17.
- Le MH, Yeo YH, Zou B, Barnett S, Henry L, Cheung R, et al. Forecasted 2040 global prevalence of nonalcoholic fatty liver disease using hierarchical bayesian approach. *Clin Molecul Hepatol*. 2022;28(4):841.
- Younossi ZM, Golabi P, Paik J, Owringi S, Yilmaz Y, El-Kassas M, et al. Prevalence of metabolic dysfunction-associated steatotic liver disease in the Middle East and North Africa. *Liver Int*. 2024;44(4):1061-70.
- Lan Y, Wang H, Weng H, Xu X, Yu X, Tu H, et al. The burden of liver cirrhosis and underlying etiologies: results from the Global Burden of Disease Study 2019. *Hepatol Commun*. 2023;7(2):e0026.
- Li B, Zhang C, Zhan YT. Nonalcoholic fatty liver disease cirrhosis: a review of its epidemiology, risk factors, clinical presentation, diagnosis, management, and prognosis. *Can J Gastroenterol Hepatol*. 2018;2018(1):2784537.
- Mantovani A, Csermely A, Petracca G, Beatrice G, Corey KE, Simon TG, et al. Non-alcoholic fatty liver disease and risk of fatal and non-fatal cardiovascular events: an updated systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(11):903-13.
- Cathcart J, Barrett R, Bowness JS, Mukhopadhyaya A, Lynch R, Dillon JF. Accuracy of Non-Invasive Imaging Techniques for the Diagnosis of MASH in Patients With MASLD: A Systematic Review. *Liver Int*. 2025;45(4):e16127.
- Selvaraj EA, Mózes FE, Jayaswal ANA, Zafarmand MH, Vali Y, Lee JA, et al. Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: A systematic review and meta-analysis. *J Hepatol*. 2021;75(4):770-85.
- Neuberger J, Patel J, Caldwell H, Davies S, Hebditch V, Hollywood C, et al. Guidelines on the use of liver biopsy in clinical practice from the British Society of Gastroenterology, the Royal College of Radiologists and the Royal College of Pathology. *Gut*. 2020;69(8):1382-403.
- Castera L, Friedrich-Rust M, Loomba R. Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2019;156(5):1264-81. e4.
- Tsai E, Lee TP. Diagnosis and evaluation of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis, including non-invasive biomarkers and transient elastography. *Clin Liver Dis*. 2018;22(1):73-92.
- Kaswala DH, Lai M, Afdhal NH. Fibrosis assessment in nonalcoholic fatty liver disease (NAFLD) in 2016. *Dig Dis Sci*. 2016;61:1356-64.
- Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. *Ann Med*. 2011;43(8):617-49.
- Imajo K, Kessoku T, Honda Y, Tomeno W, Ogawa Y, Mawatari H, et al. Magnetic resonance imaging more accurately classifies steatosis and fibrosis in patients with nonalcoholic fatty liver disease than transient elastography. *Gastroenterology*. 2016;150(3):626-37. e7.
- Cox B, Trasolini R, Galts C, Yoshida EM, Marquez V. Comparing the performance of Fibrosis-4 and Non-Alcoholic Fatty Liver Disease Fibrosis Score with transient elastography scores of people with non-alcoholic fatty liver disease. *Can Liver J*. 2021;4(3):275-82.
- Kjaergaard M, Lindvig KP, Thorhauge KH, Andersen P, Hansen JK, Kastrup N, et al. Using the ELF test, FIB-4 and NAFLD fibrosis score to screen the population for liver disease. *J Hepatol*. 2023;79(2):277-86.
- Mohammadi M, Aminian K, Joukar F, Rajabnia M, Rahmani K, Doostian A, et al. Diagnostic value of serologic biomarkers for the detection of liver fibrosis in non-alcoholic fatty liver disease. *Casp J Int Med*. 2025;16(2):275.
- Priego-Parra B, Triana-Romero A, Bernal-Reyes R, Icaza-

ETHICAL CONSIDERATIONS:

This study is the result of the thesis of Dr. Parinaz Shariati, with the ethical code R.IAU.MSHD. REC.1401.154.

CONFLICT OF INTEREST:

The authors declare no conflict of interest related to this work.

- Chávez M, Martínez-Vázquez S, Amieva-Balmori M, et al. Comparative evaluation of APRI, FIB-4, HFS, and NFS: Scoring tools for liver fibrosis in a Mexican population with MASLD. *Revista de Gastroenterología de México* (English Edition). 2024;89(4):498-505.
23. Sung S, Al-Karaghoul M, Tam M, Wong YJ, Jayakumar S, Davyduke T, et al. Age-dependent differences in FIB-4 predictions of fibrosis in patients with MASLD referred from primary care. *Hepatol Comm*. 2025;9(1):e0609.
 24. Amernia B, Moosavy SH, Banookh F, Zoghi G. FIB-4, APRI, and AST/ALT ratio compared to FibroScan for the assessment of hepatic fibrosis in patients with non-alcoholic fatty liver disease in Bandar Abbas, Iran. *BMC Gastroenterol*. 2021;21(1):453.
 25. Ghazizadeh H, Fazilati M, Pasdar A, Avan A, Tayefi M, Ghasemi F, et al. Association of a vascular endothelial growth factor genetic variant with serum VEGF level in subjects with metabolic syndrome. *Gene*. 2017;598:27-31.
 26. Joshi SR, Anjana RM, Deepa M, Pradeepa R, Bhansali A, Dhandania VK, et al. Prevalence of dyslipidemia in urban and rural India: the ICMR-INDIAB study. *PLoS One*. 2014;9(5):e96808.
 27. Lauer MS, Fontanarosa PB. Updated guidelines for cholesterol management. *JAMA*. 2001;285(19):2508-9.
 28. Hagström H, Talbäck M, Andreasson A, Walldius G, Hammar N. Repeated FIB-4 measurements can help identify individuals at risk of severe liver disease. *J Hepatol*. 2020;73(5):1023-9.
 29. Chan WK, Petta S, Nouredin M, Goh GBB, Wong VWS. Diagnosis and non-invasive assessment of MASLD in type 2 diabetes and obesity. *Alim Pharmacol Ther*. 2024;59:S23-S40.
 30. Ajmera V, Cepin S, Tesfai K, Hofflich H, Cadman K, Lopez S, et al. A prospective study on the prevalence of NAFLD, advanced fibrosis, cirrhosis and hepatocellular carcinoma in people with type 2 diabetes. *J Hepatol*. 2023;78(3):471-8.
 31. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. *Nature Rev Gastroenterol Hepatol*. 2018;15(1):11-20.
 32. Graupera I, Thiele M, Serra-Burriel M, Caballeria L, Roulot D, Wong GLH, et al. Low accuracy of FIB-4 and NAFLD fibrosis scores for screening for liver fibrosis in the population. *Clin Gastroenterol Hepatol*. 2022;20(11):2567-76. e6.
 33. Bril F, McPhaul MJ, Caulfield MP, Clark VC, Soldevilla-Pico C, Firpi-Morell RJ, et al. Performance of plasma biomarkers and diagnostic panels for nonalcoholic steatohepatitis and advanced fibrosis in patients with type 2 diabetes. *Diabetes Care*. 2020;43(2):290-7.
 34. Petta S, Wong VW-S, Bugianesi E, Fracanzani AL, Cammà C, Hiriart J-B, et al. Impact of obesity and alanine aminotransferase levels on the diagnostic accuracy for advanced liver fibrosis of noninvasive tools in patients with nonalcoholic fatty liver disease. *J Am Coll Gastroenterol ACG*. 2019;114(6):916-28.
 35. Kim RG, Deng J, Reaso JN, Grenert JP, Khalili M. Noninvasive fibrosis screening in fatty liver disease among vulnerable populations: impact of diabetes and obesity on FIB-4 score accuracy. *Diabet Care*. 2022;45(10):2449-51.
 36. Iruzubieta P, Mayo R, Mincholé I, Martínez-Arranz I, Arias-Loste MT, Ibañez-Samaniego L, et al. One-step non-invasive diagnosis of metabolic dysfunction-associated steatohepatitis and fibrosis in high-risk population. *Uni Eur Gastroenterol J*. 2024;12(7):919-29.
 37. Park H, Yoon EL, Ito T, Jo AJ, Kim M, Lee J, et al. Diagnostic performance of the fibrosis-4 Index and nonalcoholic fatty liver disease fibrosis score in lean adults with nonalcoholic fatty liver disease. *JAMA network open*. 2023;6(8):e2329568-e.
 38. Lee J, Vali Y, Boursier J, Spijker R, Anstee QM, Bossuyt PM, et al. Prognostic accuracy of FIB-4, NAFLD fibrosis score and APRI for NAFLD-related events: a systematic review. *Liver Int*. 2021;41(2):261-70.
 39. Chen M, Guo C, Ouyang K, Liu N. Diagnostic role of the fibrosis-4 index and nonalcoholic fatty liver disease fibrosis score as a noninvasive tool for liver fibrosis scoring. *Medicine*. 2024;103(43):e40214.
 40. Siddiqui MS, Yamada G, Vuppalachchi R, Van Natta M, Loomba R, Guy C, et al. Diagnostic accuracy of noninvasive fibrosis models to detect change in fibrosis stage. *Clin Gastroenterol Hepatol*. 2019;17(9):1877-85. e5.
 41. 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):1486-501.
 42. Boursier J, Guillaume M, Leroy V, Irlès M, Roux M, Lannes A, et al. New sequential combinations of non-invasive fibrosis tests provide an accurate diagnosis of advanced fibrosis in NAFLD. *J Hepatol*. 2019;71(2):389-96.
 43. Berzigotti A, Tsochatzis E, Boursier J, Castera L, Cazzagon N, Friedrich-Rust M, et al. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis—2021 update. *J Hepatol*. 2021;75(3):659-89.
 44. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 2023;77(5):1797-835.