Original Research

Fibrosis-4 index utility for screening liver fibrosis and its association with degenerative complications in patients with type 2 diabetes mellitus: a monocentric study

Hanae Rachedi[1], Abdessamad Malki[1], Alou Moussa Baraya[1], Nisrine Bouichrat[1,2], Siham Rouf[1,2], Hanane Latrech[1,2]

1) Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy, University of Mohammed 1st, Oujda, Morocco

2) Laboratory of Epidemiology, Clinical Research and Public Health, Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy, University of Mohammed 1st, Oujda, Morocco

Abstract

Backgrounds. The fibrosis-4 index is a simple biomarker tool widely recommended to diagnose advanced hepatic fibrosis in patients with type 2 diabetes mellitus (T2DM). The primary aim of this study was to assess liver fibrosis risk among type 2 diabetes mellitus patients using the Fib-4 score, secondary to compare the prevalence of degenerative complications between patients according to Fib-4 index risk, and to evaluate the prevalence of metabolic dysfunction-associated-steatotic liver disease in our population.

Methods. This is a descriptive-analytical cross-sectional study including 600 patients with type 2 diabetes mellitus who were followed at the Endocrinology-Diabetology and Nutrition Department of a university hospital center, for a period of 8 years and 10 months from January 2016 to October 2024.

Results. The mean age in our population was 59±12.8 years. The median duration of diabetes was 6.4 years (1–15 years) with a median HbA1c value of 10.2±2.7%. Overweight and obesity were found in 39.2% and 34.5% of patients respectively, with a mean BMI of 28.2±5.9 kg/m². The median of fibrosis-4 index was 1.09. Sixty-one percent of patients had a low risk of advanced liver fibrosis, 31% had an intermediate risk, and 8% had a high risk to develop an advanced liver fibrosis. Patients with a Fib-4 score ≥1.3 (indicating intermediate to high risk of liver fibrosis) had a statistically significantly higher prevalence of all microvascular complications and ischemic heart disease ($p<0.001$) compared to those with a Fib-4<1.3. There was no significant difference in HbA1c, arterial hypertension, metabolic syndrome, and dyslipidemia. However, the mean LDL-cholesterol was lower in the group with a Fib-4≥1.3 (p:0.024). Liver ultrasonography showed signs of metabolic dysfunction-associated steatotic liver disease in 47.7% of cases.

Conclusion. Fibrosis-4 index should be considered for routine screening of liver fibrosis in patients with type 2 diabetes mellitus. This simple and cost-effective tool can help identify patients at high risk. The current study highlighted the benefits of using this score among patients with T2DM and supported the high prevalence of microvascular complications and ischemic heart disease among patients with Fib-4 index ≥1.3. Furthermore prospective studies are required to evaluate the incidence outcomes in this population.

Keywords: fibrosis-4 index, non-invasive tests, type 2 diabetes mellitus, metabolic dysfunction-associated steatotic liver disease, liver fibrosis, degenerative complications

DOI: 10.15386/mpr-2954

Manuscript received: 02.12.2025
Received in revised form: 25.03.2026
Accepted: 02.04.2026

Address for correspondence:
Hanane Latrech
hlatrech@hotmail.fr

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License https://creativecommons.org/licenses/by-nc-nd/4.0/

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) previously known as non-alcoholic fatty liver disease (NAFLD) is an emerging public health issue of great interest. It ranges from simple hepatic steatosis without fibrosis, to steatohepatitis with metabolic dysfunction (MASH), which may lead to liver fibrosis, advanced cirrhosis, or even to hepatocellular carcinoma. It is commonly coexisting with type 2 diabetes mellitus (T2DM), with an increasing prevalence worldwide [1]. T2DM markedly alters glucose and lipid metabolism, leading to systemic insulin resistance, ectopic lipid accumulation, and chronic inflammation, all of which contribute to hepatic steatosis and fibrogenesis. The bidirectional relationship between T2DM and MASLD indicates that T2DM not only exacerbates MASLD progression to advanced fibrosis, but also increases the risk of both hepatic and extrahepatic complications. Conversely, MASLD itself is associated with a higher risk of developing T2DM and may further worsen glycemic control in individuals with pre-existing diabetes [2,3].

Differentiation of MASH from simple steatosis and assessment of advanced hepatic fibrosis are the key issues in MASLD patients. Liver biopsy remains the gold standard investigation to identify these two critical endpoints. However, it has many limitations including invasiveness, poor acceptability, sampling variability, cost, time-consuming and potentially life-threatening complications [4]. This situation has prompted the development of non-invasive alternatives, which have been extensively researched over the last decade [5]. A comprehensive understanding of the advantages and limitations of actually available biomarkers is imperative for selecting the appropriate biomarker for evaluating and managing patients with MASLD.

One of the non-invasive approaches is the Fibrosis-4 index. It is a simple biomarker used as a tool for diagnosing advanced hepatic fibrosis. Its calculation requires knowledge of age, ALT, and AST transaminases, and platelets count [6]. Nevertheless, several studies have reported reduced sensitivity of this index in patients with diabetes, raising concerns about the risk of missed advanced fibrosis in this population [7,8].

The primary aim of this study was to assess liver fibrosis risk among patients with type 2 diabetes mellitus using the Fib-4, and the second aim was to compare the prevalence of degenerative complications between patients according to Fib-4 risk and to evaluate the prevalence of metabolic dysfunction-associated steatotic liver disease in our population.

Methods

Participants

This was a descriptive-analytical, cross-sectional, single-center study involving 600 patients with T2DM. The study was conducted in the department of endocrinology-diabetology and nutrition at a university hospital center and covered a period of 8 years and 10 months from January 2016 to October 2024.

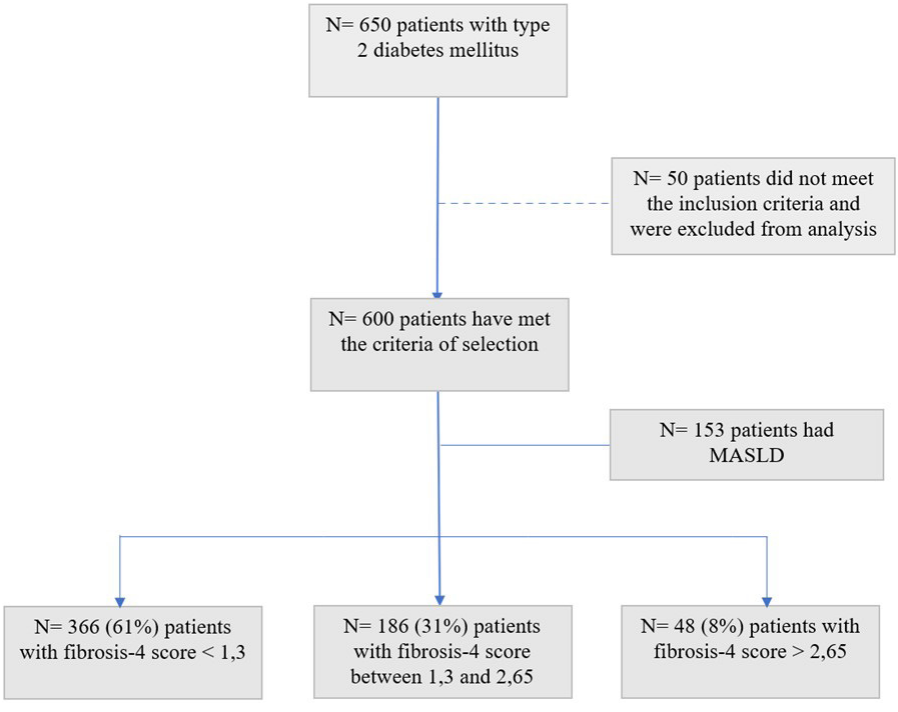

Figure 1. The study population.

The Fib-4 score was calculated in all patients with complete medical records. We have excluded from analysis all patients with incomplete data and the ones with evidence of other chronic liver diseases including hepatitis B, hepatitis C, autoimmune hepatitis (AIH), alcoholic liver disease, or risky alcohol consumption (>30 g/day for men and >20 g/day for women). In addition, patients with other pathologies that could be responsible for hepatic steatosis (e.g. hypothyroidism, severe undernutrition, hypopituitarism), pregnancy and breastfeeding, and active smoking were excluded too. From 650 patients with T2DM who were followed up during the study period, we included 600 patients following the inclusion and exclusion criteria (Figure 1).

Study design

All patients included in this study were followed and managed by specialists with recognized expertise in Endocrinology and Diabetology at our institution. The Fib-4 was calculated for all of them based on the following formula:

$$FIB-4 = \frac{Age\ (years) \times AST\ (\mathrm{U/L})}{Platelet\ count\ (10^9/\mathrm{L}) \times \sqrt{\mathrm{ALT}\ (\mathrm{U/L})}}$$

With aspartate aminotransferase (AST) and alanine aminotransferase (ALT) measured on the same day and platelets within ±30 days.

The normal ranges of serum ALT and AST were 0-55 U/L and 5-34 U/L, respectively, and a platelet count of 150.000–400.000/μL was the normal range.

Advanced liver fibrosis was assessed using the Fibrosis-4 index, with cut-off values interpreted based on the European Association for the Study of the Liver (EASL) guidelines for non-invasive fibrosis assessment [9–11].

» Fib-4 less than 1.3: low likelihood of advanced fibrosis.

» Fib-4 between 1.3 and 2.67: intermediate likelihood of advanced fibrosis or cirrhosis, additional diagnostic tests are required for confirmation.

» Fib-4 greater than 2.67: high likelihood of advanced fibrosis or cirrhosis, consideration for liver biopsy or other diagnostic tests for confirmation.

We then divided our study population into two groups based on the Fibrosis-4 score cutoff of 1.3, which distinguishes patients at low risk of liver fibrosis (<1.3) from those at intermediate to high risk (≥1.3). We then compared their anthropometric and laboratory data, as well as their degenerative complications.

Study protocol

We collected socio-demographic parameters (age, sex), co-morbid conditions, duration of diabetes, physical examination (weight, height, body mass index (BMI), waist circumference) from medical records. The presence of chronic diabetic complications was also recorded, including macrovascular complications (ischemic heart disease, ischemic stroke, and peripheral arterial disease) and microvascular complications (diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy), as documented in the patients' medical files.

Blood tests results, including liver enzymes levels, platelets count, lipid profile including total cholesterol; high-density lipoprotein cholesterol (HDL-c); low-density lipoprotein cholesterol (LDL-c); and triglycerides (TG), HbA1c, serum creatinine, and serum 25-hydroxy vitamin D levels were obtained from medical files and the hospital information system.

A liver ultrasound was performed to screen for hepatic steatosis, and the Fibrosis-4 index was used as a non-invasive tool to assess liver fibrosis.

Objectives

The primary objective was to assess liver fibrosis risk among patients with T2DM using the Fib-4 score as a non-invasive tool. The secondary aim was to compare degenerative complications status between patients according to Fib-4 score, another outcome was to determine the prevalence of MASLD among this population.

Statistical analysis

Continuous and parametric values were expressed as mean ± standard deviation, and the non-parametric variables as median (first quartile-third quartile).

The Statistical Package for the Social Sciences, version 21, was used for all analyses. The association between Fib-4 score and certain factors (e.g. metabolic syndrome, arterial hypertension, dyslipidemia and degenerative complications) was analyzed using the Student t-test and the chi-square test. p values ≤0.05 were regarded as statistically significant.

Ethics approval

The patients were informed and consented to be included in the study. The data were collected anonymously. This study is registered in the Research registry under the number: researchregistry7700 and was approved by the Ethics Board Committee of Biomedical Research at our local faculty (CERBO) under the number: 16/2020.

Results

Six hundred patients were included in the final analysis with 393 females (65.5%), and 207 males (34.5%). The mean age in our population was 59±12.8 years (with extremes from 19 to 91 years). The median duration of diabetes was 6.4 years (1–15 years) with an average HbA1c value of 10.2±2.7% (range from 5% to 19.8%). Overweight and obesity were found in 39.2% and 34.5% of patients respectively, with a mean BMI of 28.2±5.9 kg/m².

Degenerative complications were dominated by microvascular complications in 38.7% of cases, with a predominance of diabetic nephropathy (24.6%).

Macrovascular complications were identified in 36.8% of our patients, with a predominance of coronary artery disease (31.1%). Arterial hypertension was observed in 43.2% of patients. Metabolic syndrome was found in 64.7% of cases. The general characteristics of our population are presented in the table below (Table I).

Table I. General characteristics of the study participants.

	Values
Age (years)	59 ± 12.8
Gender N (%)	
* Male	207 (34.5)
* Female	393 (65.5)
HbA1c (%)	10.2 ± 2.7
Diabetes duration (years)	9.4 (1-15)
Body mass index (kg/m²)	28.2 ± 5.9
AST (UI/L)	19 (15-27)
ALT (UI/L)	17 (13-25)
Platelet count (*10⁹/L)	257.1 ± 88.3
Metabolic syndrome N (%)	388 (64.7)
Macrovascular complications N (%)	221 (36.8)
Microvascular complications N (%)	232 (38.7)

N - number, AST - aspartate aminotransferase, ALT - alanine aminotransferase.
Data are presented as mean ± SD, median (25–75th percentile), or percentages.

The Fib-4 was calculated in all our patients, with a median of 1.09 (with extremes of 0.21 to 15.9). Sixty-one percent of patients had a low risk of advanced liver fibrosis, 31% had an intermediate risk, and 8% had a high risk of developing advanced liver fibrosis. Otherwise, 321 patients (53.5%) underwent a liver ultrasonography that showed signs of MASLD in 47.7% of cases.

A comparative analysis was conducted between two groups: patients at intermediate to high risk of advanced liver fibrosis (Fib-4≥1.3), and those at low risk (Fib-4<1.3). The results showed that patients with Fib-4 above 1.3 were statistically significantly older, had a longer diabetes duration, more elevated transaminases and creatininemia levels, and a lower platelet count compared to those with scores below 1.3.

There was no significant difference in HbA1c, arterial hypertension, metabolic syndrome, and dyslipidemia. By contrast, the mean of LDL-cholesterol was lower in the group with a Fib-4 index ≥1.3 (p: 0.024).

Microvascular complications were found in 47.6% of patients with a Fib-4 greater than 1.3 (vs 32.9% in the group with a Fib-4 <1.3) predominated by diabetic nephropathy in 33.9% of cases. There was a statistically significant correlation between the Fib-4 index ≥1.3 and the prevalence of all microvascular complications.

Table II. Comparison of anthropometric and laboratory data in patients according to fibrosis-4 score.

	Fib-4< 1.3 (N= 366)	Fib-4 ≥ 1.3 (N= 234)	P values
Age (years)	54.9 ± 12.5	65.2 ± 10.8	***<0.001***
Hba1c (%)	10.4 ± 2.6	9.9 ± 2.8	*0.062*
Diabetes duration (years)	6 (1-1.8)	10 (1.9-17)	***0.004***
AST (UI/L)	17 (14-21.5)	25 (19-36)	***<0.001***
ALT (UI/L)	16 (12-22)	19 (14-29.3)	***0.003***
Platelet count (*10⁹/L)	291± 84.2	204.3 ± 66.1	***<0.001***
Cholesterol (g/l)	1.7 ± 0.5	1.6 ± 0.5	***0.046***
Triglyceride (g/l)	1.5 ± 0.9	1.4 ± 1	*0.462*
HDL (g/l)	0.4 ± 0.1	0.4 ± 0.2	*0.567*
LDL (g/l)	1.1 ± 0.6	1 ± 0.4	***0.024***
BMI (kg/m²)	28.4 ± 6.2	27.8 ± 5.4	*0.260*
Abdominal circumference (cm)	98.5 ±13.6	98.4 ± 14.3	*0.969*
Hypertension N (%)	153 (41.9)	105 (44.9)	*0.500*
Dyslipidemia N (%)	119 (32.6)	91 (38.9)	*0.132*
Metabolic syndrome N (%)	237 (64.9)	150 (64.1)	*0.817*
Macrovascular complications:			
Ischemic heart disease N (%)	78 (21.4)	107 (45.9)	***<0.001***
Ischemic stroke N (%)	20 (5.5)	14 (6)	*0.779*
Obliterative arteriopathy of the lower limbs N (%)	21 (5.8)	13 (5.6)	*0.826*
Microvascular complications :			
Diabetic retinopathy N (%)	69 (19)	67 (28.8)	***0.007***
Diabetic nephropathy N (%)	68 (18.7)	79 (33.9)	***<0.001***
Diabetic neuropathy N (%)	44 (12.2)	45 (19.3)	***0.021***
Creatininemia (mg/l)	9.8 ± 8.4	11.9 ± 10.8	***<0.001***
Serum 25-hydroxy vitamin D (ng/ml)	15.1 ± 8.4	14.5 ± 8.5	*0.351*
MASLD confirmed on liver ultrasonography N: 153 (%)	96 (62.7)	57 (37.3)	*0.557*

N - number, AST - aspartate aminotransferase, ALT - alanine aminotransferase, HbA1c - hemoglobin A1c.
Data are presented as mean ± SD, median (25–75th percentile), or percentages.
The comparisons were analyzed using the t-student test and chi-square test. A value of p<0.05 indicated significance.

Macrovascular complications were observed in 50% of patients with a Fib-4 ≥1.3 (vs 28.2% in patients with a Fib-4 <1.3) predominated by ischemic heart disease in 45.9% of cases with a significant correlation between Fib-4 index ≥1.3 and the prevalence of ischemic heart disease ($p < 0.001$; r: 0.256).

Among patients older than 65 years, by using the Fib-4 score cut-off of 1.3, 39.7% were classified as low risk, 45.7% as intermediate risk, and 14.6% as high risk for advanced liver fibrosis. When the cut-off was adjusted to 2 in accordance with current guidelines that recommend a higher cut-off of 2 for the Fib-4 index in the elderly population, the proportion of patients in the intermediate zone decreased to 13.6%.

All anthropometric and biological data of the two study groups are presented in the table II.

To manage MASLD in our population, a multidisciplinary approach with coordination between the departments of endocrinology-diabetology-nutrition and hepato-gastro-enterology was used. It was based on dietary interventions with physical activity, evaluation and adjustment of antidiabetic and anti-lipid medications, assessment of degenerative complications, and management of comorbidities and associated cardiovascular risk factors. All patients with a high risk of advanced liver fibrosis have been referred to a specialized hepato-gastro-enterology consultation.

Discussion

MASLD and T2DM are commonly coexisting. Their association is complex and bidirectional, and it has been linked to an increased risk of developing advanced liver fibrosis, cirrhosis, and hepatocellular carcinoma [12]. Hepatic steatosis is usually identified using liver ultrasonography, which is the initial noninvasive imaging modality for detecting MASLD in clinical practice due to its accessibility and costeffectiveness. Despite its high diagnostic accuracy for detecting moderate to severe hepatic steatosis (≥30% liver fat), its sensitivity is lower in cases of mild steatosis (<30% liver fat) [13]. In the present study, 53,5% of patients underwent liver ultrasonography, which revealed signs of MASLD in 47,7% of cases in the examined subgroup, highlighting the high prevalence of this condition in patients with T2DM.

In comparison to existing studies, a meta-analysis of 123 studies (N = 2.224.144 patients with T2DM) reported a global MASLD prevalence of 65.3% in this population. The prevalence increased from 55.86% in 1990–2004 to 68.81% in 2016–2021. Eastern Europe had the highest MASLD prevalence among patients with T2DM, followed by the Middle East, while the lowest prevalence was recorded in Africa [14]**.** Another meta-analysis of seventeen studies involving 10.897 patients with T2DM reported an overall MASLD prevalence of 54% in this population [15].

Identifying patients with advanced liver fibrosis or cirrhosis, which are at high risk of developing complications, is the main challenge in clinical practice. Liver biopsy remains the gold standard for staging liver fibrosis. However, it appears practically difficult to realize for all high-risk patients. This has encouraged the development of alternative non-invasive approaches, which have been the subject of massive research over the last decade. Although none of the non-invasive tests can adequately discriminate MASH from simple steatosis in patients with MASLD [16], they are now widely used in liver clinics for the detection of advanced liver fibrosis and are recommended by international guidelines [17]. The Fib-4 index, represents the first line of non-invasive tools in current recommendations. It was initially developed to evaluate liver fibrosis in patients with hepatitis C/human immunodeficiency virus co-infection [17]. It is now recommended by several international guidelines as the first step in assessing liver fibrosis in patients with type 2 diabetes mellitus. It is a reliable and affordable parameter, the calculation of which is widely accessible and based on routinely measured blood tests (age, AST, ALT, and platelet count). Because the Fib-4 shows a high negative predictive value (NPV) for detecting advanced fibrosis, it is recommended to exclude people who do not have advanced fibrosis before moving on to a second-tier test. However, it also has several drawbacks, including the overpredicting risk of liver fibrosis in older patients because its formula includes age [18,19]. In this regard, many studies have reported that using Fib-4 score in elderly patients may increase the false positive rate [20,21]. As a result, several guidelines reported the upper cut-off of 2 in the Fib-4 in patients over 65 years while the existing thresholds should continue to be used in patients aged 35–65 years. In the present study, we observed that utilizing an upper cut-off value of 2 significantly reduced the percentage of patients aged over 65 who fell into the grey zone. The grey zone rate dropped to 13.6% when the age-adjusted Fib-4 threshold was applied, compared to 45.7% when using the cut-off value of 1.3.

Using the new cutoffs for elderly patients may offer a better patient classification, helping avoid unnecessary and potentially invasive investigations while reducing costs through fewer inappropriate referrals.

Our patients with a Fib-4 score ≥1.3 exhibited a statistically significantly higher prevalence of all microvascular complications and ischemic heart disease. Consistent with our findings, multiple studies have reported similar associations. For instance, Papanas et al [22] recently demonstrated that patients with Fib-4≥1.3 had markedly higher rates of chronic vascular complications, including peripheral neuropathy, chronic kidney disease, retinopathy, stroke, coronary artery disease, and peripheral arterial disease; moreover, Fib-4 correlated with greater neuropathy severity. Saito et al [23] found that Fib-4≥1.3 had prognostic value for diabetic kidney disease and proteinuria

in patients with type 2 diabetes mellitus. Similarly, Zhang et al [24] reported a strong association between Fib-4 and both diabetic kidney disease and its progression in this population. Erdogan et al [25] also observed a significantly higher prevalence of diabetic nephropathy among patients with Fib-4 ≥1.3.

Additionally, Fib-4 appears to be associated with increased cardiovascular mortality [26]. In our study, patients with Fib-4≥1.3 exhibited a significantly higher prevalence of ischemic heart disease than those with Fib-4<1.3. Sun et al [27] further reported that elevated Fib-4 levels were independently associated with myocardial infarction risk, particularly among females and those with hypertension.

The strengths of our study include, to the best of our knowledge, that it is the first in our country to estimate the risk of liver fibrosis among patients with type 2 diabetes using the Fib-4 index. We also evaluate the degenerative status of patients with a positive score and assess the effect of age on the performance of the Fib-4 index.

We acknowledge that our study has some limitations that require consideration. First, this is a single-center study. However, it includes a considerable number of patients with T2DM recruited from all parts of the eastern region of our country. Second, in this study, liver ultrasonography was not available for all patients, because it was not used as an inclusion criterion in the study, since the assessment of MASLD prevalence was a secondary objective. Despite this limitation, the prevalence of MASLD in the examined subgroup remained considerable highlighting the high prevalence of this condition in patients with T2DM. Third, we enrolled a cross-sectional analysis based on retrospective data and the present findings reflect prevalent and non-incident outcomes which led us to initiate a prospective study to overcome this limitation.

Conclusion

In conclusion, using non-invasive methods to screen for liver fibrosis in patients with T2DM should be considered as an essential approach of their routine evaluation. Fibrosis-4 score can serve as a simple and cost-effective tool for identifying patients at high risk of liver fibrosis. Despite the limitations, the study findings highlighted the benefits of using this score among patients with T2DM and supported the high prevalence of microvascular complications and ischemic heart disease among patients with Fib-4 index ≥1.3. Further prospective studies are required to evaluate the incidence outcomes in these population.

Acknowledgments

The authors would like to acknowledge all medical and paramedical staff involved in the management of the patients and the patients' families for their cooperation and patience.

References

1. Zhou JH, Cai JJ, She ZG, Li HL. Noninvasive evaluation of nonalcoholic fatty liver disease: Current evidence and practice. World J Gastroenterol. 2019;25:1307-1326. doi: 10.3748/wjg.v25.i11.1307.
2. Cusi K, Abdelmalek MF, Apovian CM, Balapattabi K, Bannuru RR, Barb D, et al. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association. Diabetes Care. 2025;48:1057-1082. doi: 10.2337/dci24-0094.
3. 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. doi: 10.1016/j.jhep.2023.06.003.
4. Castera L, Friedrich-Rust M, Loomba R. Noninvasive Assessment of Liver Disease in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019 Apr;156(5):1264-1281.e4. doi:10.1053/j.gastro.2018.12.036
5. 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. doi: 10.1016/j.jhep.2015.04.006.
6. Mallet V, Parlati L, Vallet-Pichard A, Terris B, Tsochatzis E, Sogni P, et al. L'index FIB-4 pour faire le diagnostic de fibrose hépatique avancée au cours de la stéatose hépatique [FIB-4 index to rule-out advanced liver fibrosis in NAFLD patients]. Presse Med. 2019;48:1484-1488. French. doi: 10.1016/j.lpm.2019.10.017.
7. Boursier J, Hagström H, Ekstedt M, Moreau C, Bonacci M, Cure S, et al. Non-invasive tests accurately stratify patients with NAFLD based on their risk of liver-related events. J Hepatol. 2022;76:1013-1020. doi: 10.1016/j.jhep.2021.12.031.
8. Gracen L, Hayward KL, Irvine KM, Valery PC, Powell EE. Low accuracy of FIB-4 test to identify people with diabetes at low risk of advanced fibrosis. J Hepatol. 2022;77:1219-1221. doi: 10.1016/j.jhep.2022.06.016.
9. Wattacheril JJ, Abdelmalek MF, Lim JK, Sanyal AJ. AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review. Gastroenterology. 2023;165:1080-1088. doi: 10.1053/j.gastro.2023.06.013.
10. 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. doi: 10.1016/j.jhep.2021.05.025.
11. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024;81:492-542. doi: 10.1016/j.jhep.2024.04.031.

12. Bondini S, Kleiner DE, Goodman ZD, Gramlich T, Younossi ZM. Pathologic assessment of non-alcoholic fatty liver disease. Clin Liver Dis. 2007;11:17-23, vii. doi: 10.1016/j.cld.2007.02.002.
13. Tamaki N, Ajmera V, Loomba R. Non-invasive methods for imaging hepatic steatosis and their clinical importance in NAFLD. Nat Rev Endocrinol. 2022;18:55-66. doi: 10.1038/s41574-021-00584-0.
14. Younossi ZM, Golabi P, Price JK, Owrangi S, Gundu-Rao N, Satchi R, et al. The Global Epidemiology of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis Among Patients With Type 2 Diabetes. Clin Gastroenterol Hepatol. 2024;22:1999-2010.e8. doi: 10.1016/j.cgh.2024.03.006.
15. Amiri Dash Atan N, Koushki M, Motedayen M, Dousti M, Sayehmiri F, Vafaee R, et al. Type 2 diabetes mellitus and non-alcoholic fatty liver disease: a systematic review and meta-analysis. Gastroenterol Hepatol Bed Bench. 2017;10:S1-S7.
16. 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. doi: 10.1016/j.jhep.2015.04.006.
17. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006;43:1317-1325. doi: 10.1002/hep.21178.
18. Joo SK, Kim W, Kim D, Kim JH, Oh S, Lee KL, et al. Steatosis severity affects the diagnostic performances of noninvasive fibrosis tests in nonalcoholic fatty liver disease. Liver Int. 2018;38:331-341. doi: 10.1111/liv.13549.
19. Ishiba H, Sumida Y, Seko Y, Tanaka S, Yoneda M, Hyogo H, et al. Type IV Collagen 7S Is the Most Accurate Test For Identifying Advanced Fibrosis in NAFLD With Type 2 Diabetes. Hepatol Commun. 2020;5:559-572. doi: 10.1002/hep4.1637.
20. McPherson S, Hardy T, Dufour JF, Petta S, Romero-Gomez M, Allison M, et al. Age as a Confounding Factor for the Accurate Non-Invasive Diagnosis of Advanced NAFLD Fibrosis. Am J Gastroenterol. 2017;112:740-751. doi: 10.1038/ajg.2016.453.
21. Ishiba H, Sumida Y, Tanaka S, Yoneda M, Hyogo H, Ono M, et al. The novel cutoff points for the FIB4 index categorized by age increase the diagnostic accuracy in NAFLD: a multicenter study. J Gastroenterol. 2018;53:1216-1224. doi: 10.1007/s00535-018-1474-y. Erratum in: J Gastroenterol. 2018;53:1225. doi: 10.1007/s00535-018-1478-7.
22. Papanas N, Gouveri E, Panou T, Trypsianis G, Papazoglou D. Association of fibrosis-index-4 (FIB-4) with chronic vascular complications of type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes 2026;134(01):19-23. doi: 10.1055/a-2765-6480
23. Saito H, Tanabe H, Kudo A, Machii N, Higa M, Yamaguchi S, et al. High FIB4 index is an independent risk factor of diabetic kidney disease in type 2 diabetes. Sci Rep. 2021 Jun;11:11753. doi: 10.1038/s41598-021-88285-6.
24. Zhang J, Chen S, Tian Z, Cao J, Jiao Y, Wang B, et al. Association Between Liver Fibrosis Score and Diabetic Kidney Disease: A Retrospective Cross-Sectional Study of Hospitalized Patients. Exp Clin Endocrinol Diabetes. 2024;132:328-335. doi: 10.1055/a-2280-3742.
25. Erdogan BT, Tam AA, Baser H, Cuhaci Seyrek FN, Polat SB, Ersoy R, et al. Relationship between fibrosis-4 score and microvascular complications in patients with type 2 diabetes mellitus. Arab J Gastroenterol. 2024;25:269-274. doi: 10.1016/j.ajg.2024.04.001.
26. Hagström H, Nasr P, Ekstedt M, Stål P, Hultcrantz R, Kechagias S. Accuracy of Noninvasive Scoring Systems in Assessing Risk of Death and Liver-Related Endpoints in Patients With Nonalcoholic Fatty Liver Disease. Clin Gastroenterol Hepatol. 2019;17:1148-1156.e4. doi: 10.1016/j.cgh.2018.11.030.
27. Sun Z, Zhang J, Duan J, Wang Q, Yun Z, Lin J, et al. Cross-sectional study on the association between the fibrosis-4 index and co-occurring myocardial infarction in Chinese patients with type 2 diabetes mellitus. Front Endocrinol (Lausanne). 2025;16:1551472. doi: 10.3389/fendo.2025.1551472.