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Original Article

Diagnostic value of serologic biomarkers for the detection of liver fibrosis in non-alcoholic fatty liver disease

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Abstract

Background: The aim of this study was to evaluate the diagnostic accuracy of various non-invasive methods for Non-alcoholic fatty liver disease (NAFLD)-diagnosis in an Iranian population. The methods studied included aspartate aminotransferase to platelet ratio index (APRI), fibrosis-4 (FIB-4) index, aspartate aminotransferase to alanine aminotransferase ratio (AAR), aspartate aminotransferase to platelet count index (AP index), fibrosis index (FI), NAFLD fibrosis score (NFS), Forns index, BARD score, BAAT score and PLALA score. The aim of the current study was to correlate these methods with liver stiffness measurement (LSM) and serum fibrosis markers, using FibroScan as the gold standard.

Methods: In a cross-sectional study of 504 patients with NAFLD or non-alcoholic steatohepatitis (NASH), FibroScan examinations were performed and demographic, clinical and biochemical data were collected. Statistical analyses evaluated the performance of each diagnostic panel, calculating sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

Results: The APRI had high specificity (97.27%) but low sensitivity (4.12%) and limited discriminatory power AUC: 0.50) in the fibrosis panel. In contrast, Forns index and NFS had better AUC values (0.64 and 0.63, respectively), with the NFS having a sensitivity of 80%, indicating potential for broad-based screening. In the cirrhosis panel, the APRI was characterized by high specificity (98.21%) but had low sensitivity (4%) and limited discriminatory power (AUC: 0.51), while the FIB-4 had the highest AUC (0.67) and a sensitivity of 60%, suggesting its efficacy as a screening tool.

Conclusion: NFS and FIB-4 showed promising performance among the evaluated panels for population screening.

Keywords: NAFLD, FibroScan, Fibrosis, FIB-4, APRI, Non-invasive, AST/ALT.

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Non-alcoholic fatty liver disease (NAFLD) is a liver disorder characterized by an excessive accumulation of fat in the liver of non-alcoholic individuals. In a subset of NAFLD patients, non-alcoholic steatohepatitis (NASH) may develop. This progression can lead to significant liver scarring and varying degrees of fibrosis, cirrhosis and impaired liver function (1, 2). Activation of the immune system and recruitment of proinflammatory cells play a crucial role in the pathogenesis of NASH (3). In liver fibrosis, components of the extracellular matrix are deposited and form stable and visible fibers within the liver parenchyma (4, 5). An imbalance of gut bacteria, known as gut dysbiosis, has been associated with NAFLD. The various stages of NAFLD are characterized by specific patterns in the gut microbiota (6). NAFLD diagnosis requires a liver steatosis of ≥5% on biopsy, which rules out other causes (7). The global prevalence of NAFLD is increasing and is estimated to be 25.2% overall, with the prevalence of NASH ranging from 1.5% to 6.5%(8) (9, 10). In Iran, the prevalence of NAFLD is estimated at 33.9% (11).

Approximately 25-40% of NAFLD patients develop NASH (12), and 5%-10% of patients develop cirrhosis, end-stage liver disease (ESLD) or hepatocellular carcinoma (HCC) (13). NAFLD is becoming a major cause of cirrhosis, HCC and is the second most common cause of liver transplantation in some regions (13, 14). Genetic factors, diabetes, obesity, and metabolic syndrome contribute significantly to NAFLD (15). Despite their impact, there are currently no approved pharmacologic therapies for the treatment of NAFLD (16). Liver biopsy, the gold standard for diagnosis, has its limitations, which has prompted the search for non-invasive biomarkers (17). Misclassification of biopsy results is characterized by a false negative/positive rate of more than 25% (4). Advanced fibrosis is defined as stage F2-F4, following the Metavir fibrosis stage (18). While liver biopsy remains necessary to identify patients with NASH and early fibrosis, it is not suitable for population-level screening (19). Imaging techniques, including ultrasound and FibroScan, play a prominent role in NAFLD assessment (20) and have a sensitivity and specificity of approximately 85% and 90%, respectively. (11). Elastography techniques assess liver stiffness by measuring the velocity of shear waves generated by a probe. These techniques have proven their reliability and reproducibility in the assessment of fibrosis in children and adolescents (21). FibroScan can be used at the bedside or in the outpatient clinic. In this method, an ultrasound probe generates an elastic shear wave through low- amplitude and low-frequency oscillations transmitted through the liver tissue. The shear wave is then transmitted using pulse-echo ultrasound, measuring the velocity (m/s) and providing an accurate measurement of liver stiffness (LSM) within a given volume of liver tissue (1). The stiffer the tissue, the faster the shear wave propagates (22). LSM is quantified in kilopascals (KPa) and correlates with the fibrosis stage (23). Normally, the mean value of ten measurements in healthy subjects is between 1.5 and 7.5 kPa, while values above 10.5 kPa indicate the presence of fibrosis and advanced fibrosis (17). However, the optimal cut-off values for detecting liver fibrosis in NAFLD patients vary widely, ranging from 5.8 to 11 kPa for significant fibrosis (stage 2), 6.95 to 11.4 kPa for advanced fibrosis (stage 3) and 7.9 to 22.3 kPa for cirrhosis (stage 4) (22). LSM results may be influenced by ALT flares, extrahepatic cholestasis, and liver congestion and are challenging in those with narrow intercostal spaces (22). Both the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) recommend the use of transient elastography, in particular FibroScan, for the assessment of liver fibrosis in NAFLD (11, 24, 25). The aim of the present study was to evaluate the diagnostic accuracy of non-invasive methods, including APRI, FIB4, AAR, AP index, FI, Forns index, BARD, BAAT, PLALA score, and NFS, in an Iranian population and to establish correlations between LSM and serum fibrosis markers, with FibroScan as the gold standard.

Methods

Participants: This cross-sectional study involved 504 patients diagnosed with NAFLD or NASH based on ultrasound findings. Participants were examined by FibroScan between October 2022 and October 2023 at the Gastroenterology Clinic of Guilan University of Medical Science in Rasht city. Ethical approval for the study was obtained from the Ethics Committee (IR.GUMS.REC.1402.519). Inclusion criteria were all patients referred to the Gastroenterology Super-Specialty Clinic of the Guilan University of Medical Sciences who were diagnosed with non-alcoholic fatty liver by ultrasound and who did not meet any exclusion criteria. Exclusion criteria included patients with viral and autoimmune hepatitis, drug-induced liver diseases, chronic liver diseases such as primary biliary cirrhosis, sclerosing cholangitis, genetic and metabolic liver diseases like hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency associated with liver disease, current or past alcohol consumption of more than 20 grams per day, signs of hepatocellular carcinoma (HCC) or liver cancer, a history of bariatric surgery.

Procedure: Each patient underwent a FibroScan (Fibroscan 502 device, operated by VCTE) to determine the degree of fibrosis (F0-F4) and steatosis (S1-S3) of the liver. Demographic characteristics, including age and gender, were recorded. Clinical and biochemical indicators such as CBC, ALT, AST, total and direct bilirubin, alkaline phosphatase, lactate dehydrogenase, triglycerides, high density lipoprotein, low density lipoprotein, total cholesterol, albumin, ferritin, total iron binding capacity, gamma-glutamyl transpeptidase, ceruloplasmin, transferrin saturation, and alpha-phytoprotein. The presence of diabetes, (patients with diabetes treated with antidiabetic drugs or with an HbA1c value of more than 6.5% or a fasting blood sugar (FBS) value of more than126 mg/d), HTN, dyslipidemia, hypothyroidism and polycystic ovary syndrome was also recorded. Serologic panels for the evaluation of liver fibrosis, along with their calculation formulas and cut-off points, include the following: 1. FIB4 panel: the formula is (age [years] × AST [U/L]) / ([PLT

(10^9/L)] × ALT [U/L]) ^1/2, cut-off points: less than 1.45 indicates no severe fibrosis, and more than 3.25 indicates severe fibrosis.

2. APRI panel: the formula: (AST / AST upper limit normal) / [platelet count (10^9/L)] × 100, cut-off point: less than 0.88 indicates the absence of severe fibrosis. A value of greater than 0.88 indicates the presence of severe fibrosis.

3. AAR panel: the formula is AST: ALT ratio, cut-off point: Equal to or greater than 0.8 indicates the presence of severe fibrosis.

4. NAFLD fibrosis score (NFS) panel: The formula is 1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m^2) + 1.13 × diabetes (yes = 1, no = 0) + (0.99 × AST/ALT ratio) + (0.013 × platelet [×10^9/L]) + (0.66 × albumin [g/dl]), cut-off points: less than -1.455 indicates no severe fibrosis, greater than 0.676 indicates severe fibrosis.

5. AP panel: formula age (years) score + platelets score, (age score: 30 = 0; 30−39 = 1; 40−49 = 2; 50−59 = 3; 60−69 = 4; ≥70 = 5), (platelets score: ≥225 = 0; 200−224 = 1; 175−199 = 2; 150−174 = 3; 125−149 = 4; <125 = 5), cut-off point: equal to or greater than 6 indicates severe fibrosis.

6. BAAT score panel: the parameters are age, BMI, ALT, triglycerides and scoring: each case with a BMI ≥ 28, an age ≥ 50 years, an ALT ≥ 80 units/liter and a triglyceride ≥ 150 mg/dL was assigned a grade, then the scores from these 4 parameters were summed, cut-off point: a score in the range of 2-4 indicates severe liver fibrosis.

7. BARD score panel: The parameters are BMI, diabetes, AST/ALT ratio, and scoring: BMI > 28 kg/m² = 1 point - AST/ALT ratio > 0.8 = 2 points- diabetes = 1 point. Cut-off point: Values of 2, 3 or 4 indicate the presence of severe fibrosis.

8. PLALA panel: The parameters are platelet, albumin, AST/ALT ratio, and scoring: score for platelets < 153,000/mm³, albumin < 4g/dL, and AST/ALT ratio ≥ 0.9, then the scores of these three parameters were added together. Cut-off point: A score ≥ 2 indicates severe fibrosis.

9. Fibrosis index (FI) panel: The formula is (albumin * 1.08) + (platelet * 0.01) - 8.28 and cut-off point: Scores greater than or equal to 2.1 indicate the presence of severe fibrosis.

10. Forns Index Panel: The formula is 7.811 – 3.131 x ln (platelet [10^9 /L]) + 0.781 x ln (GGT [IU/L]) + 3.467 x ln age – 0.014 x cholesterol [mg/dL] and cut-off points: Values greater than or equal to 6.9 indicate the presence of severe fibrosis and values less than 4.2 indicate the absence of severe fibrosis. These panels provide different parameters and scoring systems to assess liver fibrosis, each with specific cut-off points to categorize the severity of fibrosis.

Statistical analysis: In the present study, statistical methods were used to evaluate the diagnostic value of the different panels in identifying severe fibrosis in patients. Using SPSS22 software, the demographic data of two groups, those with and those without severe fibrosis, were compared. Qualitative parameters were subjected to chi-square test, while quantitative parameters were assessed using the T-test. FibroScan results were categorized into groups according to the severity of fibrosis. The results of all panels were analyzed using the t-test, with significance set at $p < 0.05$. Each panel was dichotomized into the absence or presence of severe fibrosis based on a cut-off value and compared with the Fibroscan results. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of each panel were calculated, and receiver operating characteristic (ROC) curves were generated. The panels were also compared in terms of their diagnostic performance. The aim of the current study was to provide comprehensive insight into the diagnostic capabilities of the panels in identifying severe fibrosis.

Results

A total of 504 people took part in this study. The average age of the participants was 48.22±13.41 years. The average body mass index was 30.44±5.54 kg/m. The gender distribution across the cohort was balanced and equally divided between women (252) and men (252), as shown in the following table1. There was a significant gender difference in the prevalence of significant fibrosis. Women had a higher prevalence (23.4%) compared to men (15.1%). Older people had a higher prevalence, with a mean age of 54.38 years in those with significant fibrosis compared to 46.75 years for those without. The magnitude of the p-value (0.02) suggested a strong association between age and significant fibrosis. BMI showed no statistical significant association (p-value 0.12), although individuals with significant fibrosis had a slightly higher mean BMI (31.21) than people without fibrosis (30.25). Diabetes Mellitus (DM) was associated with significant fibrosis, as indicated by the prevalence rates. Individuals with DM had a significantly higher prevalence (28.90%) compared to individuals without DM (9.27%). The magnitude of the p (<0.001) indicates a significant relationship between DM and significant fibrosis, as shown in table 2 below.

Table 1. Demographic characteristics of patients in the study

Varible	Total
Gender (F/M)	252/252
Age (year)	48.22±13.41
BMI (kg/m^2) (BMI) body mass index	30.44±5.54

Table 2. Demographic characteristics of patients with significant fibrosis

		Significant fibrosis		P-value
		Yes	No	
Gender	Female	59 (23.4%)	193 (76.6%)	0.020
	Male	38 (15.1%)	214 (84.9%)	
Age (year)		54.38±12.62	46.75±13.19	<0.001
BMI (kg/m^2)		31.21±6.91	30.25±5.15	0.120
DM	Yes	74 (28.90%)	182 (71.10%)	<0.001
	No	23 (9.27%)	225 (90.73%)	

(BMI) body mass index, (DM) diabetes mellitus

There is no significant difference in the prevalence of cirrhosis between women (5.6%) and men (4.4%). Cirrhosis is more common in older individuals. The mean age of people with cirrhosis was 58.20 years compared to 47.70 years for those without cirrhosis, and the p-value suggested a strong association. Similar average BMI values in individuals with and without cirrhosis (30.05 vs. 30.46). Higher prevalence of cirrhosis in individuals with diabetes (7.8%) compared to those without (1.97%). Age and diabetes appear to be significant factors associated with cirrhosis in this study population. Gender and BMI illustrated no significant association with cirrhosis in the analyzed data set. The prevalence of cirrhosis was significantly higher in individuals with diabetes, as indicated in table3.

The results of the panels were categorized into two groups: significant fibrosis and non-significant fibrosis, based on the cut-off values mentioned in the method. Then the comparison was made with the standard of the ongoing study, the Fibroscan device, which categorizes patients into significant fibrosis and non-significant fibrosis. Table 4 below presents the performance metrics for various fibrosis panels. These metrics provide insight into how well each panel can identify patients with significant fibrosis and those without fibrosis and help to evaluate the effectiveness of each panel in distinguishing between these two conditions. Two variants of the APRI are demonstrated in this table: APRI** covers the upper part of the fibrosis range (probable fibrosis), while APRI* covers a broader spectrum that includes possible fibrosis and probable fibrosis.

Notable features of APRI** include low sensitivity (4.12%) and high specificity (97.27%), while APRI* has sensitivity (53.61%) and specificity (61.85%). NFS** targets the upper part of the fibrosis range as a predictor of fibrosis, while NFS* covers a wider range and serves as a predictor of fibrosis and intermediate fibrosis. NFS** is characterized by low sensitivity (24.74%) and high specificity (87.96%), while NFS* has sensitivity (80.41%) and specificity (46.19%). AP has a low sensitivity (29.90%) and high specificity (83.05%), BAAT a high sensitivity (69.07%) and specificity (39.31%), BARD a high sensitivity (74.23%) and specificity (45.45%), PALA a low sensitivity (18.56%) and high specificity (86.24%), FI also a low sensitivity (9.28%) and high specificity (88.94%), Forns index a sensitivity (54.39%) and specificity (75.51%)

Table 3. Demographic characteristics of patients with cirrhosis based on demographic and clinical factors in the study

		Cirrhosis		P-value
		Yes	No	
Gender	Female	14 (5.6%)	238 (94.4%)	0.68
	Male	11 (4.4%)	241 (95.6%)	
Age (year)		58.20±12.17	47.70±13.28	<0.001
BMI (kg/m^2)		30.05±6.13	30.46±5.51	0.71
DM	Yes	20 (7.8%)	236 (92.2%)	<0.001
	No	5 (1.97%)	243 (98.13%)	

(BMI) body mass index, (DM) diabetes mellitus.

Table 4. Performance of the different fibrosis panels

Panels	Sensitivity	Specificity	PPV	NPV	Accuracy
	Total	Total	Total	Total	Total
APRI **	4.12	97.27	26.67	80.82	79.20
APRI *	53.61	61.85	25.37	84.64	60.24
NFS**	24.74	87.96	32.87	83.06	75.79
NFS*	80.41	46.19	35.62	90.82	52.77
AP	29.90	83.05	29.59	83.25	72.81
BAAT	69.07	39.31	21.34	84.21	45.03
BARD	74.23	45.45	24.49	88.09	50.99
PALA	18.56	86.24	24.32	81.63	73.21
FI	9.28	88.94	16.67	80.44	73.61
Forns Index	54.39	75.51	34.06	87.68	71.52

(APRI) aspartate aminotransferase to platelet ratio index, (AP index) aspartate aminotransferase to platelet count index, (FI) fibrosis index, (NFS) NAFLD fibrosis score, Forns index, BARD score, BAAT score and PLALA score, NPV (negative predictive value), PPV (positive predictive value).

In table 5, the results of the cirrhosis panels are categorized into two groups based on predefined cut-offs and compared with the FibroScan results. Fib-4** indicates high probability, Fib-4* covers broader possibilities, APRI** suggests probable cirrhosis and APRI* covers a broader range. FIB-4** indicates moderate sensitivity (28%) and high specificity (96.45%), PPV (29.17%) and accuracy (93.68%). FIB-4* has a high sensitivity (60%), specificity (75.57%), PPV (11.36%) and accuracy (74.75%). APRI** demonstrates low sensitivity (4%), high specificity (98.52%), NPV (95.10%) and accuracy (93.77%). APRI* shows moderate sensitivity (40%), high specificity (83.51%), PPV (11.36%) and accuracy (80.88%). AAR reveals moderate sensitivity (48%), high specificity (68.06%), PPV (7.27%) and accuracy (66.99%).

Table 6 provides the area under the curve (AUC) values for different fibrosis panels, evaluating their performance in discrimination between significant and non-significant fibrosis. Here are the AUC values for each fibrosis panel in the total population. The best AUC values were for NFS *: (AUC = 0.63) and AP: (AUC = 0.56) and BARD: (AUC = 0.59) and Forns index: (AUC = 0.64). The visual meaning of the above tables can be found in figure1 to 4. In table 7, the best AUC for cirrhosis panels was for FIB-4*: (AUC = 0.67). The visual significance of the above panels is shown in figure 5.

Table 5. Illustrates the performance metrics, including sensitivity, specificity

Panels	Sensitivity	Specificity	PPV	NPV	Accuracy
	Total	Total	Total	Total	Total
FIB-4**	28	96.45	29.17	96.25	93.05
FIB-4*	60	75.57	11.36	97.31	74.80
APRI**	4	98.52	14.28	95.10	93.77
APRI*	40	83.51	11.36	96.34	81.32
AAR	48	68.06	7.27	96.16	67.06

NPV (negative predictive value), PPV (positive predictive value) and accuracy, calculated for various cirrhosis panels. Fibrosis-4 (FIB4) index, (APRI) aspartate aminotransferase to platelet ratio index, (AAR) alanine aminotransferase ratio.

Table 6. The AUC values for the different fibrosis panels

Fibrosis Panels	AUC of Total
APRI **	0.50
APRI *	0.57
NFS**	0.56
NFS*	0.63
AP	0.56
BAAT	0.54
BARD	0.59
PALA	0.52
FI	0.49
Forns Index	0.64

(APRI) aspartate aminotransferase to platelet ratio index, (NFS) NAFLD fibrosis score, (AP) aspartate aminotransferase to platelet count index, BARD score, BAAT score, PLALA Score, (FI) fibrosis index, Forns index

Table 7. Illustrates the AUC values for the different cirrhosis panels

Cirrhosis panels	AUC of Total
FIB-4**	0.62
FIB-4*	0.67
APRI **	0.51
APRI *	0.61
AAR	0.58

(FIB-4) fibrosis-4 index, (APRI) aspartate aminotransferase to platelet ratio index, (AAR) alanine aminotransferase ratio

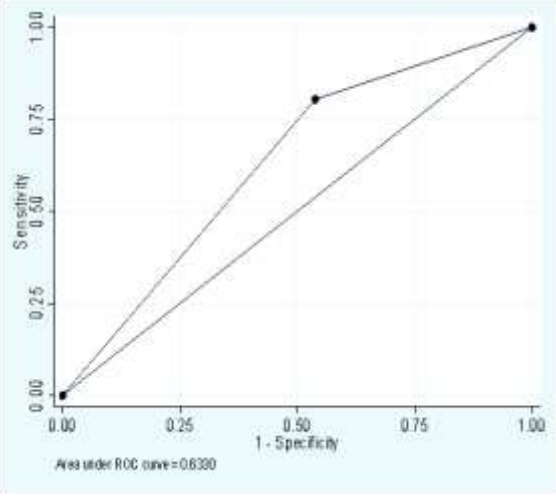

Figure 1. AUC for NFS* in fibrosis, (NFS) NAFLD Fibrosis Score

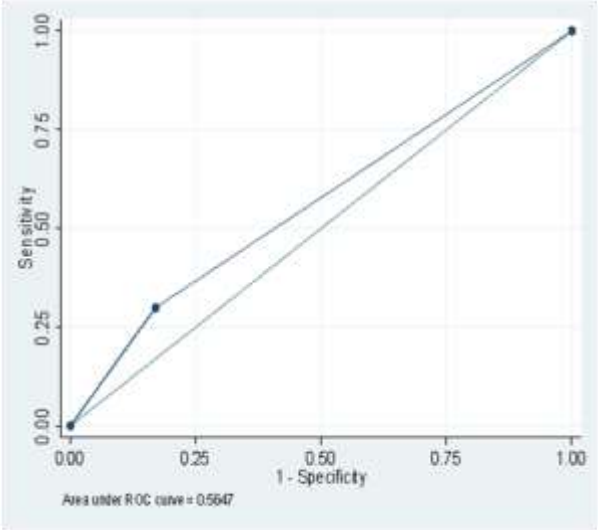

Figure 2. AUC for AP in fibrosis, (AP) aspartate aminotransferase to platelet count index

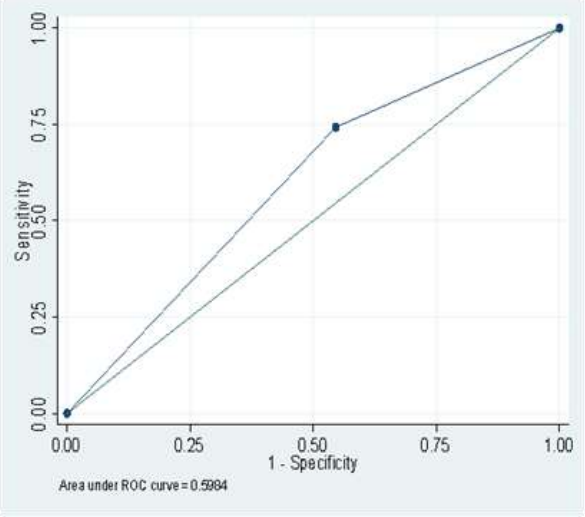

Figure 3. AUC for BARD in fibrosis, BARD score

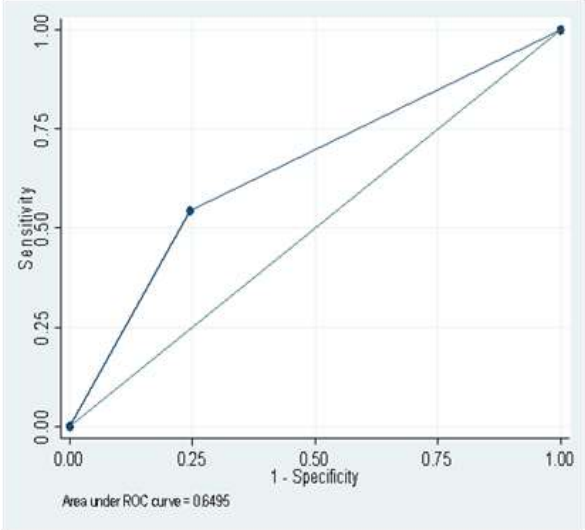

Figure 4. AUC for the Forn index in fibrosis

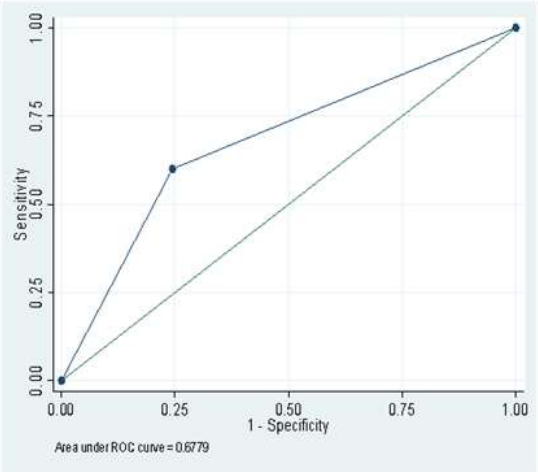

Figure 5. AUC for the FIB-4* in cirrhosis, (FIB-4) fibrosis-4 index

Discussion

In a meta-analysis conducted by Sergio et al., in which 46,514 participants, the AUC values for various non-invasive markers were as follows: APRI for advanced fibrosis and cirrhosis (AUC: 0.72), FIB-4 for advanced fibrosis (AUC: 0.81) and cirrhosis (AUC: 0.83), NFS for advanced fibrosis (AUC: 0.81) and cirrhosis (AUC: 0.69), and BARD score for advanced fibrosis (AUC: 0.73). These findings are consistent with the results of our study (26).

The results of the present study are again consistent with those of a separate study investigating the diagnostic accuracy of APRI and FIB-4 together with other non-invasive methods for the detection of advanced fibrosis. In a meta-analysis by Xiao et al. (27), which involved more than 13,000 patients, APRI was assessed using two thresholds, similar to our study. At APRI thresholds of 1.0 and 1.5, sensitivities and specificities for fibrosis of as 50.0%, 84.0%, 18.3%, and 96.1%, respectively, were reported. In the current study, the APRI** indicated the highest specificity (97.27%) for fibrosis evaluation, indicating a low false-positive rate, but its sensitivity was notably low (4.12%), suggesting a higher false-negative rate. Moreover, APRI** demonstrated limited discriminatory ability (AUC: 0.50). The AUC values for the diagnosis of fibrosis using APRI, FIB-4, BARD score, NFS and FibroScan were reported as 0.77, 0.84, 0.76, 0.84, and 0.88, respectively, in the meta-analysis by Xiao et al. In contrast, in the ongoing study, the Forns index and the NFS* had better AUC values (0.64 and 0.63, respectively), with the NFS* having the highest sensitivity (80%), indicating its potential for broad-based screening. Furthermore, FIB-4* had the highest AUC value (0.67) and higher sensitivity (60%). The discrepancy in AUC values between the studies may be due to differences in the gold standards used. In the present study, FibroScan was used as the gold standard, while in the other study liver biopsy was used. NFS and Fib-4 were also suggested as recommendations in the cross-sectional study conducted in Portugal (20). In a cross-sectional study by Siddiqui MS et al. involving 292 subjects in which two biopsies were performed along with accompanying laboratory data, it was found that FIB-4, APRI, and NFS were able to detect advanced fibrosis and progression of fibrosis in patients with NAFLD, which is consistent with the results of the present study (28). The common feature of these three panels (FIB-4, APRI, and NFS) was the ratio of AST to ALT.

NFS and FIB-4 are valuable screening methods that are suitable for routine use in the clinical setting. They effectively exclude individuals with advanced fibrosis and offer cost-effectiveness and ease of access (19). Liver biopsy, despite its utility, is limited by its costliness and the potential for sampling error and inter-observer variability, leading to misclassification of fibrosis stages (29). Different parts of the liver may be in different stages of fibrosis or the experience of the pathologists becomes an influential factor in the assessment of fibrosis (11). Therefore, despite their limited diagnostic power, clinicians often resort to biochemical and imaging tests to mitigate the risks associated with biopsy (17). A liver biopsy accounts for only 1/50,000 of the liver volume. Consequently, biopsies from different areas may represent different stages of fibrosis, with cirrhosis potentially being missed in up to 30% of patients, with a 1% risk of significant post-biopsy complications such as bleeding, injury to adjacent organs, bile leakage and infection (1).

Indeed, it is reasonable to consider replacing biopsy with FibroScan to broaden the scope of work and collect more data from the population. Transient elastography was

approved by the FDA in the United States in 2013. Liver biopsy, despite its cost, is subject to sampling error and interobserver variability, leading to misclassification of fibrosis stage. The expertise of the pathologists influences fibrosis assessment. As a result, clinicians often rely on biochemical and imaging tests to minimize the risks of biopsy despite their limitations. Liver biopsy samples represent only a small portion of the liver volume, so cirrhosis can be missed in up to 30% of cases and there is a 1% risk of complications. A combined approach of non-invasive serum markers and transient elastography is proposed for fibrosis assessment, with biopsy reserved for cases requiring further investigation. One of the strengths of the study is the relatively good representativeness of the study population. However, one of the limitations is the lack of a very strong gold standard. Nevertheless, the adoption of FibroScan as the gold standard allows for a broader study population. Recommendations for future studies include the inclusion of multi-centers, liver biopsy as the gold standard, and expansion of the study population. The novelty of this study lies in the establishment of correlations between liver stiffness measurement (LSM) and serum fibrosis markers. In fibrosis, the NFS* panel has a high sensitivity of 80% of patients. Its relatively good AUC values (0.63) make it more suitable for population screening compared to other panels. In cirrhosis, the FIB-4* panel has a high sensitivity of 60%, and its relatively good AUC values (0.67) make it more suitable for population screening than other panels.

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