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Araştırma Makalesi

The diagnostic performance of non-invasive fibrosis markers for predicting fibrosis in primary biliary cholangitis patients

Primer biliyer kolanjit hastalarında fibrozisi öngörmede invaziv olmayan fibrozis belirteçlerinin tanısal performansı

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Abstract

Aim: This study aimed to investigate the relationship between liver fibrosis measured by transient elastography and non-invasive fibrosis scoring systems, including Fibrosis-4 (FIB-4) and aspartate-aminotransferase (AST)-to-platelet ratio index (APRI), in patients with primary biliary cholangitis (PBC).

Material and Methods: A total of 45 PBC patients followed in the Gastroenterology Clinic were included in this retrospective study. Transient elastography was performed on all participants, and liver stiffness measurement (LSM) values were recorded in kilopascals (kPa). Fibrosis was defined as LSM ≥ 6.3 kPa, while advanced fibrosis was defined as LSM ≥ 10.5 kPa. To calculate the APRI score, the formula [(AST / upper normal limit × 100) / platelet count] was used, and for the FIB-4 score, the formula [(age × AST) / (platelet count × √alanine aminotransferase)] was applied.

Results: Liver fibrosis was identified in 71.1% (n = 32) of patients, with advanced fibrosis present in 40.0% (n = 18). Patients with fibrosis had higher APRI and FIB-4 scores compared to those without fibrosis. Also, the median APRI score (0.7 vs. 0.5, $p < 0.001$) and median FIB-4 score (2.4 vs. 1.6, $p < 0.001$) were higher in patients with advanced liver fibrosis than in those without. For detecting fibrosis, the AUROC values were 0.73 (95% CI: 0.58–0.89) for APRI and 0.84 (95% CI: 0.73–0.96) for FIB-4. FIB-4 also showed higher accuracy than APRI for identifying advanced fibrosis (AUROC: 0.78 vs. 0.70, $p = 0.048$).

Conclusion: Both APRI and FIB-4 are useful non-invasive tools for detecting and staging fibrosis in PBC. However, FIB-4 demonstrated superior diagnostic performance compared to APRI, particularly in predicting advanced fibrosis. Incorporating these markers into routine clinical practice may reduce the need for invasive liver biopsy and help optimize patient management.

Keywords: Primary biliary cholangitis, transient elastography, liver fibrosis, FIB-4 score, APRI score

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Öz

Amaç: Bu çalışma, primer biliyer kolanjit (PBC) hastalarında transient elastografi ile ölçülen karaciğer fibrozisi ile Fibrozis-4 (FIB-4) ve aspartat-aminotransferaz-trombosit oranı indeksi (APRI) gibi non-invaziv fibrozis skorlama sistemleri arasındaki ilişkiyi araştırmayı amaçladı.

Gereç ve Yöntemler: Gastroenteroloji Kliniği'nde takip edilen toplam 45 PBC hastası bu retrospektif çalışmaya dahil edildi. Tüm katılımcılara transient elastografi uygulandı ve karaciğer sertliği ölçüm (LSM) değerleri kilopaskal (kPa) cinsinden kaydedildi. Fibrozis, LSM ≥ 6.3 kPa olarak tanımlanırken, ileri fibrozis LSM ≥ 10.5 kPa olarak kabul edildi. APRI skorunun hesaplanmasında [(AST / üst normal sınır × 100) / trombosit sayısı] formülü, FIB-4 skorunun hesaplanmasında ise [(yaş × AST) / (trombosit sayısı × √alanin aminotransferaz)] formülü uygulandı.

Bulgular: Hastaların %71.1'inde (n = 32) karaciğer fibrozisi, %40.0'ında (n = 18) ise ileri fibrozis saptandı. Fibrozisi olan hastalarda ibrozisi olmayan hastalara kıyasla APRI ve FIB-4 skorları f daha yüksekti. İleri fibrozisi olan hastalarda ileri fibrozis olmayan hastalara kıyasla da APRI (0.7 vs. 0.5, p < 0.001) ve FIB-4 (2.4 vs. 1.6, p < 0.001) skorları daha yüksekti. Fibrozisin saptanmasında, AUROC değerleri APRI için 0.73 (%95 GA: 0.58–0.89) ve FIB-4 için 0.84 (%95 GA: 0.73–0.96) olarak bulundu. FIB-4, ileri fibrozisi belirlemede de APRI'ye göre daha yüksek doğruluk gösterdi (AUROC: 0.78 karşı 0.70, p = 0.048).

Sonuçlar: APRI ve FIB-4, PBC hastalarında fibrozis tespiti ve evrelemesi için kullanışlı non-invaziv araçlardır. Bununla birlikte, FIB-4 özellikle ileri fibrozisi öngörmede APRI'ye kıyasla üstün tanısal performans sergilemiştir. Bu belirteçlerin rutin klinik uygulamalara dahil edilmesi, invaziv karaciğer biyopsisi ihtiyacını azaltabilir ve hasta yönetimini optimize etmeye yardımcı olabilir.

Anahtar Kelimeler: Primer biliyer kolanjit, transient elastografi, karaciğer fibrozisi, FIB-4 skoru, APRI skoru

Introduction

Primary biliary cholangitis (PBC) is an autoimmune disease that causes gradual destruction of the intrahepatic bile ducts, increased inflammation in the periportal area, and cholestasis (1, 2). It was previously known as primary biliary cirrhosis. Although genetic factors are blamed for the etiology of PBC, environmental factors are also thought to play a role (3, 4). It is frequently seen in women between the ages of 30 and 60. In the USA, the incidence of PBC is estimated to be 45 per million in women and 7 per million in men, and the prevalence is 654 per million in women and 121 per million in men (5-7). rolonged cholestasis associated with PBC can progress to cirrhosis and portal hypertension, underscoring the need for accurate fibrosis assessment (8).

Liver fibrosis, rather than bile duct loss, is considered a more reliable marker of histological progression in PBC. Liver biopsy is the gold standard for evaluating fibrosis, but its invasive nature, associated risks, and patient discomfort limit its routine use (9). non-invasive alternatives, such as the aspartate-aminotransferase-to-platelet ratio index (APRI), Fibrosis-4 (FIB-4) score, and imaging methods like transient elastography, have gained traction for diagnosing and monitoring fibrosis in PBC. Many studies have found that transient elastography provides a higher diagnostic performance in the differential diagnosis of fibrosis (10-14). However, transient elastography has limitations, including high cost and limited availability in many healthcare systems. In contrast, APRI and FIB-4 are cost-effective, easy-to-calculate, and widely applicable, offering a more accessible alternative for fibrosis evaluation (15, 16). Despite their lower diagnostic accuracy compared to transient elastography, their affordability and simplicity make them valuable tools in clinical practice.

The current literature provides limited findings on the diagnostic performance of these scoring systems in PBC patients. Therefore, this study aimed to investigate the relationship between liver fibrosis measured by transient elastography and non-invasive fibrosis scoring systems, including FIB-4 and APRI, in PBC patients.

Material and Methods

This retrospective study was conducted with PBC patients who admitted to the Gastroenterology Clinic of the Umraniye Training and Research Hospital. The present study adhered to the ethical regulations and principles as stipulated in the Declaration of Helsinki. The study received approval from the

Ethical Committee of the Umraniye Training and Research Hospital, Clinical Research Ethics Committee (Date: 02.11.2023, Decision No. B.10.1.TKH.4.34.H.GP.0.01/412). The requirement for obtaining informed consent was exempted by the Ethics Committee, given the retrospective design of the study.

Study population

The study enrolled 45 patients diagnosed with PBC, monitored at the Liver Clinic from January 2016 to October 2021, and who had transient elastography performed. PBC was diagnosed in patients with elevated alkaline phosphatase (ALP) if one of the following criteria was met: positivity for antimitochondrial antibodies (AMA) or histopathological evidence of non-suppurative destructive cholangitis with interlobular bile duct damage [7]. Exclusion criteria comprised individuals under 18, those with decompensated cirrhosis confirmed clinically, radiologically, or through laboratory findings, patients with pacemakers, those with ascites, those with pregnant women, those with alcohol consumption, those with viral hepatitis, and those with missing transient elastography data or incomplete records. Data on demographic information (age, gender, waist circumference, height, weight, body mass index (BMI)), clinical characteristics (comorbidities, duration of PBC), and laboratory findings were retrieved from patient records.

Laboratory parameters

Blood samples for routine analyses, including complete blood count and biochemical parameters, were taken from the antecubital vein of all patients at the Liver Clinic following at least 8 hours of fasting. All analyses are performed in the same laboratory using consistent equipment. Non-invasive fibrosis scores are calculated using the demographic and laboratory data obtained (17-19):

$$\text{APRI} = \frac{\text{AST (U/L)}}{\text{upper limit of normal AST (U/L)}} \times 100 \div \text{Platelets } (\text{x}10^9/\text{L})$$

$$\text{FIB} - 4 = \frac{Age \times \text{Aspartate aminotransferase (AST; U/L)}}{\sqrt{\text{Alanine aminotransferase (ALT; U/}L) \times \text{Platelets } (\text{x}10^9/\text{L})}}$$

Transient elastography

Transient elastography was conducted by a single operator using the FibroScan® Compact 530 device (Echosens SA, Paris, France). Participants were instructed to fast for at least 3 hours prior to the assessment. The procedure was performed with participants lying in the supine position, with their right arm fully abducted. The M probe was used for all examinations, and the XL probe was employed when indicated by the automatic probe selection tool. Only measurements with at least 10 valid readings and an interquartile range (IQR) to median ratio of <30% were considered reliable.

Liver stiffness measurement (LSM) values were recorded in kilopascals (kPa) , while controlled attenuation parameter (CAP) values, obtained simultaneously, were measured using the second-generation CAP (CAPc) and expressed in dB/m. The procedure was continued until CAP values were achieved for 100% of measurements (20). Fibrosis was considered present at LSM ≥ 6.3 kPa, while advanced fibrosis was defined as LSM ≥ 10.5 kPa (20).

Statistical analysis

All statistical analyses were conducted using STATA/MP v.16 software (StataCorp LLC, Texas, USA). Numerical data with a normal distribution, as determined by the Kolmogorov-Smirnov test, are presented as mean ± standard deviation, whereas non-normally distributed variables are expressed as median (25th-75th percentiles). Comparisons between two groups were performed using the Student t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. For comparisons involving more than two groups, the ANOVA test (post-hoc: Bonferroni) was used for normally distributed data, and the Kruskal-Wallis H test (post-hoc: Dunn's test) was used for non-normally distributed data. Categorical variables were summarized as numbers and percentages, with group comparisons performed using the Chi-square test or Fisher's exact test when applicable. A multivariable logistic regression analysis employing the backward Wald method was used to identify potential independent predictors of fibrosis. The diagnostic performance of non-invasive fibrosis scores was evaluated through receiver operating characteristic (ROC) curve analysis, with the area under the curve (AUC), standard error (SE), sensitivity, and specificity reported. The optimal cutoff values for predicting fibrosis were determined using the Youden index method. A p-value of $P < 0.05$ was considered statistically significant for all analyses.

Results

The study population consisted of 45 patients with a mean age of 60.2 ± 9.4 years, the majority of whom were female. The mean disease duration was 5.4 ± 1.8 years. The demographic and clinical findings of the patients are detailed in Table 1. Liver fibrosis was detected in 71.1% of cases (n = 32), with advanced liver fibrosis present in 40.0% (n = 18). The ratio of hypertension was higher in patients with liver fibrosis than in

those without (59.4% vs. 15.4%, p = 0.009). Other demographic characteristics did not show significant differences between the groups with and without liver fibrosis. The median AST and ALT levels were similar in patients with and without liver fibrosis, but mean platelet levels were lower in those with fibrosis. The median APRI score (0.5 vs. 0.3, p = 0.015) and median FIB-4 score (1.9 vs. 1.0, p < 0.001) were higher in in patients with liver fibrosis than in those without (Table 1).

The demographic characteristics were comparable between patients with and without advanced fibrosis. While platelet and AST values did not differ significantly, the median AST level was higher in patients with advanced fibrosis. The median APRI score (0.7 vs. 0.5, p < 0.001) and median FIB-4 score (2.4 vs. 1.6, p < 0.001) were higher in patients with advanced liver fibrosis than in those without (Table 2).

The diagnostic performance of the APRI and FIB-4 scores in predicting fibrosis was evaluated using ROC curve analysis. The area under the ROC curve (AUROC) for APRI in detecting fibrosis was 0.73 (95% CI: 0.58-0.89), while for FIB-4, the AUROC was 0.84 (95% CI: 0.73-0.96). The FIB-4 score demonstrated superior diagnostic performance in predicting fibrosis compared to the APRI score (AUC: 0.84 vs. 0.73, p < 0.001) (Figure 1) (Table 3).

Table 1. The demographic and clinical findings of patients with primary biliary cholangitis.

Variables	All population n=45	Fibrosis		p
		No n=13	Yes n=32	
Age, years	60.2 ± 9.4	54.8 ± 10.0	62.3 ± 8.4	0.014*
Gender, n (%)				
Female	39 (86.7)	11 (84.6)	28 (87.5)	0.999
Male	6 (13.3)	2 (15.4)	4 (12.5)	
WC, cm	95.6 ± 12.4	90.1 ± 11.2	97.9 ± 12.3	0.054
BMI, kg/m2	29.3 ± 5.8	28.2 ± 5.7	29.8 ± 5.9	0.404
Hypertension, n (%)	21 (46.7)	2 (15.4)	19 (59.4)	0.009*
Diabetes mellitus, n (%)	10 (22.2)	2 (15.4)	8 (25.0)	0.698
Disease duration, years	5.4 ± 1.8	5.4 ± 1.8	5.3 ± 1.9	0.728
TE findings				
CAP score, dB/m	227.8 ± 49.9	216.2 ± 39.0	232.5 ± 53.6	0.328
Fibrosis score, kpa	8.6 (6.3-14.3)	5.7 (5.6-6.2)	11.8 (8.4-18.4)	<0.001*
Laboratory findings				
Glucose, mg/dL	94.0 (86.0-101.0)	92.0 (88.0-99.0)	94.5 (85.0-102.0)	0.688
Albumin, g/L	42.5 ± 3.6	43.2 ± 1.9	42.2 ± 4.1	0.405
Platelets, x109/L	216.2 ± 77.3	268.9 ± 55.4	194.7 ± 75.1	0.002*
HDL-C, mg/dL	54.0 (47.0-63.0)	54.0 (49.0-61.0)	54.5 (46.5-65.2)	0.634
LDL-C, mg/dL	118.9 ± 30.5	135.7 ± 34.0	112.1 ± 26.5	0.017*
Triglyceride, mg/dL	104.0 (76.0-136.0)	103.0 (91.0-136.0)	107.0 (74.5-134.2)	0.861
AST, U/L	24.0 (20.0-32.0)	25.0 (22.0-30.0)	23.5 (20.0-34.5)	0.661
ALT, U/L	20.0 (14.0-31.0)	20.0 (14.0-25.0)	21.5 (13.8-31.2)	0.725
IgG, g/L	13.9 (12.2-15.8)	12.2 (10.1-14.0)	14.1 (12.5-16.8)	0.082
IgM, g/L	1.8 (1.3-2.4)	1.8 (1.4-1.9)	1.7 (1.3-2.7)	0.745
GGT, U/L	51.0 (24.0-107.0)	51.0 (22.0-82.0)	50.0 (25.5-114.5)	0.698
Total bilirubin, mg/dL	0.6 ± 0.3	0.5 ± 0.2	0.6 ± 0.3	0.107
Sodium, mEq/L	140.5 ± 2.8	140.4 ± 2.2	140.6 ± 3.1	0.832
AFP, ng/mL	142.0 (114.0-179.0)	125.0 (114.0-144.0)	152.0 (119.5-181.2)	0.150
Creatinine, mg/dL	0.8 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	0.100
CRP, mg/L	4.9 (2.1-6.3)	4.0 (1.8-5.4)	5.1 (3.0-8.8)	0.106
APRI score	0.4 (0.3-0.6)	0.3 (0.2-0.4)	0.5 (0.3-0.6)	<0.001*
FIB-4 score	1.8 (1.2-2.4)	1.0 (0.9-1.5)	1.9 (1.5-3.2)	<0.001*

Data are mean ± standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: AFP, alpha fetoprotein; ALT, alanine aminotransferase, AST, aspartate aminotransferase, ALP, alkaline phosphatase; BMI, body mass index; CAP, controlled attenuation parameter; CRP, C-reactive protein; GGT, gamma glutamyl transferase; IgG, immunoglobulin G, IgM, immunoglobulin M; TE, transient elastography

Table 2. Demographic and clinical findings associated with advanced fibrosis.

Variables	Fibrosis			p
	No n=13	No advanced n=14	Advanced n=18	
Age, years	54.8 ± 10.0	62.2 ± 5.7	62.4 ± 10.1	0.050*
Gender, n (%)				
Female	11 (84.6)	13 (92.9)	15 (83.3)	0.264
Male	2 (15.4)	1 (7.1)	3 (16.7)	
WC, cm	90.1 ± 11.2	94.4 ± 13.7	100.7 ± 10.7	0.060
BMI, kg/m2	28.2 ± 5.7	28.1 ± 5.4	31.1 ± 6.1	0.239
Hypertension, n (%)	2 (15.4)	7 (50.0)	12 (66.7)	0.018*
Diabetes mellitus, n (%)	2 (15.4)	3 (21.4)	5 (27.8)	0.712
Disease duration, years	5.5 ± 1.8	5.0 ± 1.7	5.5 ± 2.1	0.851
TE findings				
CAP score, dB/m	216.2 ± 39.0	236.5 ± 61.7	229.3 ± 48.0	0.576
Fibrosis score, kpa	5.8 ± 0.4	8.2 ± 1.2	23.3 ± 10.8	<0.001*
Laboratory findings				
Glucose, mg/dL	94.3 ± 11.1	94.6 ± 10.2	110.6 ± 34.5	0.210
Albumin, g/L	43.2 ± 1.9	43.3 ± 1.8	41.3 ± 5.1	0.206
Platelets, x109/L	268.9 ± 55.4	206.6 ± 58.6	185.5 ± 66.3	0.008*
HDL-C, mg/dL	54.0 (49.0-61.0)	60.5 (52.5-69.0)	49.0 (44.2-56.8)	0.131
LDL-C, mg/dL	135.7 ± 34.0	112.4 ± 31.6	111.8 ± 22.8	0.059
Triglyceride, mg/dL	103.0 (91.0-136.0)	114.5 (71.5-127.8)	104.0 (76.5-143.5)	0.921
AST, U/L	25.8 ± 10.0	23.2 ± 5.5	45.3 ± 10.8	0.025*
ALT, U/L	20.0 (14.0-25.0)	21.5 (13.2-24.0)	23.0 (14.2-50.5)	0.621
IgG, g/L	12.6 ± 4.1	12.9 ± 2.4	17.2 ± 4.5	0.016
IgM, g/L	1.8 (1.4-1.9)	1.8 (1.3-2.3)	1.7 (1.3-4.1)	0.845
GGT, U/L	51.0 (22.0-82.0)	39.5 (14.0-81.5)	67.5 (30.2-149.0)	0.219
Total bilirubin, mg/dL	0.5 ± 0.2	0.6 ± 0.2	0.7 ± 0.3	0.068
Sodium, mEq/L	140.4 ± 2.2	141.0 ± 2.1	140.2 ± 3.7	0.730
AFP, ng/mL	125.0 (114.0-144.0)	141.0 (108.5-166.8)	163.5 (136.2-249.5)	0.083
Creatinine, mg/dL	0.7 ± 0.1	0.8 ± 0.2	0.8 ± 0.2	0.246
CRP, mg/L	4.0 (1.8-5.4)	3.3 (2.1-6.2)	5.8 (3.9-9.0)	0.112
APRI score	0.3 (0.2-0.4)	0.5 (0.3-0.5)	0.7 (0.4-0.9)	<0.001*
FIB-4 score	1.0 (0.9-1.5)	1.6 (1.4-2.1)	2.4 (1.9-3.9)	<0.001*

Data are mean ± standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Differences between groups are highlighted in bold characters. Abbreviations: AFP, alpha fetoprotein; ALT, alanine aminotransferase, AST, aspartate aminotransferase, ALP, alkaline phosphatase; BMI, body mass index; CAP, controlled attenuation parameter; CRP, C-reactive protein; GGT, gamma glutamyl transferase; IgG, immunoglobulin G, IgM, immunoglobulin M; TE, transient elastography.

Table 3. Diagnostic performance of the aspartate amino-transferase-to-platelet ratio index APRI), and fibrosis score 4 (FIB-4) for distinguishing fibrosis.

ROC curve findings	APRI	FIB-4
Fibrosis vs. no fibrosis		
AUC	0.73	0.84
Standard Error	0.08	0.06
95% CI	0.58-0.89	0.73-0.96
Sensitivity	53.0	88.0
Specificity	92.3	69.2
Cut-off value	0.45	1.33
Advanced fibrosis vs. no advanced fibrosis		
AUC	0.70	0.78
Standard Error	0.09	0.08
95% CI	0.53-0.86	0.58-0.89
Sensitivity	40.0	77.2
Specificity	100.0	72.4
Cut-off value	0.60	1.80

Abbreviations: APRI, aspartate aminotransferase to platelet ratio index; AUC, area under the curve; CI, confidence interval; FIB-4: fibrosis-4 score.

The area under the ROC curve (AUROC) for APRI in detecting advanced fibrosis was 0.70 (95% CI: 0.53-0.86), while for FIB-4, the AUROC was 0.78 (95% CI: 0.58-0.89). The FIB-4 score demonstrated superior diagnostic performance in predicting fibrosis compared to the APRI score (AUC: 0.78 vs. 0.70, p = 0.048) (Figure 1) (Table 3).

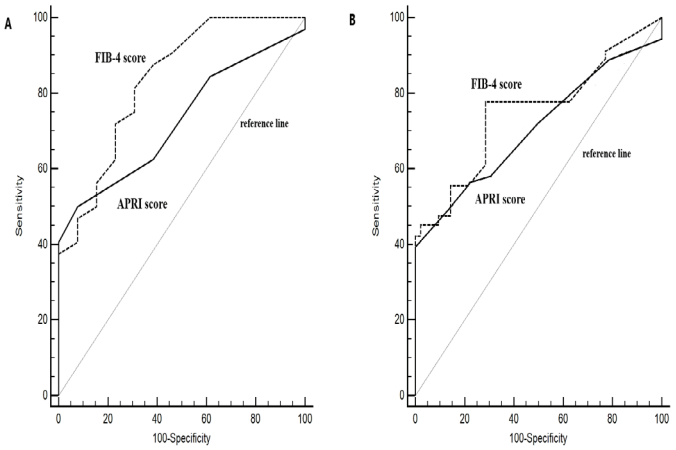

Figure 1. The diagnostic performance of the APRI and FIB-4 scores in predicting presence (A) and advanced (B) fibrosis.

Discussion

To the best of our knowledge, this study is among the few that investigate the correlation between fibrosis measured by transient elastography and non-invasive fibrosis scoring systems in in patients with PBC. In the present study, we evaluated the diagnostic accuracy of non-invasive fibrosis markers in patients with PBC. Our findings demonstrated that both APRI and FIB-4 scores were higher among patients with liver fibrosis, as well as in those with advanced fibrosis. Furthermore, FIB-4 showed a superior diagnostic performance compared to APRI for detecting both presence and advanced fibrosis.

PBC typically presents more frequently in women aged between 40 and 60 years, and patients are often diagnosed in middle to older age (21, 22).The mean age of our cohort and the predominance of women align with previously reported demographic profiles. The study identified a higher prevalence of hypertension in the fibrotic group. In a study examining cardiac function and morphology in non-cirrhotic PBC patients, it was reported that PBC, when compared to age-matched controls, is linked to higher blood pressure, heart remodeling, and functional abnormalities (23). While the precise mechanisms connecting hypertension to PBC-related fibrosis are not yet fully understood, systemic comorbidities like hypertension are frequently associated with chronic liver diseases and may indicate elevated vascular resistance or portal hypertension in advanced stages. However, further research is needed to determine whether hypertension arises directly from liver-related pathophysiological changes or shares common underlying risk factors.

In accordance with the literature, platelet levels were lower in patients with fibrosis, likely due to hypersplenism and increased platelet sequestration secondary to portal hypertension (24). Although AST and ALT levels did not differ significantly between those with and without fibrosis, we found that AST levels were higher among patients with advanced fibrosis, suggesting a more pronounced hepatocellular injury (25). Advanced fibrosis is associated with increased risk of complications such as portal hypertension and cirrhosis, emphasizing the importance of early and accurate fibrosis detection.

A study by Corpechot et al. showed that elastography outperformed non-invasive scores in identifying advanced fibrosis and cirrhosis, while APRI and FIB-4 exhibited comparable diagnostic performance (26). The challenges of elastography include its unavailability in many clinics, as well as the additional costs and time required. This underscores the importance of more affordable and easily accessible non-invasive fibrosis markers. Non-invasive tools such as APRI and FIB-4, which have been extensively validated in chronic viral hepatitis and non-alcoholic fatty liver disease, are increasingly being explored in cholestatic conditions like PBC (27, 28). In our study, both APRI and FIB-4 effectively predicted the presence and advanced

fibrosis. FIB-4 demonstrated higher AUROC values compared to APRI for identifying both fibrosis and advanced fibrosis. FIB-4 index integrates age, AST, ALT, and platelet count, capturing multiple components of fibrogenesis. This may explain its particular effectiveness in predicting advanced fibrosis. In contrast, APRI, which relies solely on AST levels and platelet counts, provides a more limited perspective—yet remains valuable due to its simplicity and low cost. However, the current literature contains conflicting findings regarding the diagnostic performance of these indices. A study by Li and colleagues on PBC patients demonstrated AUROC values of 0.65 for APRI and 0.72 for FIB-4 in predicting advanced fibrosis (28). A study involving 107 PBC patients identified erythrocyte distribution width, FIB-4, albumin, and platelet levels as fibrosis-associated markers, with FIB-4 demonstrating the greatest sensitivity and specificity for differentiating histological severity (26). In a study conducted by Ölmez et al. involving 40 PBC patients, APRI and FIB-4 scores were found to be higher in patients with early and advanced-stage fibrosis. However, While the APRI score had a higher AUROC value than the FIB-4 score, the difference was not statistically significant (0.75 vs. 0.69, respectively) (29). In a study conducted by Sayar et al. involving 53 PBC patients, APRI and FIB-4 scores were reported to show no differences between early and advanced fibrosis groups (16). Variations between studies could be attributed to differences in patient selection.

From a clinical standpoint, our results highlight the significant advantage of using these non-invasive indices to assess the stage of fibrosis without requiring a liver biopsy. The invasive nature of biopsy, along with the risk of complications such as bleeding and patient discomfort, increasingly drives the search for reliable non-invasive alternatives. The high sensitivity and specificity of FIB-4 make it a particularly valuable tool for guiding treatment decisions and monitoring disease progression in PBC. Identifying patients at higher risk of developing advanced fibrosis or cirrhosis at earlier stages can help clinicians tailor more intensive therapeutic strategies.

One major limitation of this study is the relatively small sample size, predominantly consisting of female patients, which may restrict the generalizability of our findings. Second, the cross-sectional design limits the ability to assess temporal changes in fibrosis markers or their prognostic value over time. Additionally, liver biopsy, the gold standard for diagnosing and staging fibrosis, was not utilized in this study. Lastly, the study did not account for all potential confounders, such as co-existing conditions (e.g. alcohol consumption, or viral hepatitis), which could influence fibrosis progression or the values of non-invasive markers. Future prospective studies with larger cohorts and multifaceted evaluations are needed to establish more comprehensive data in this field.

Conclusion

This study confirms the diagnostic utility of non-invasive markers such as APRI and FIB-4 for predicting both the presence and severity of fibrosis in patients with PBC. FIB-4, in particular, demonstrated superior performance and may reduce the need for invasive liver biopsy in routine practice. The integration of non-invasive approaches benefits clinicians by enabling earlier detection of fibrosis progression and helping guide timely therapeutic interventions. Hence, the use of tools like FIB-4 and APRI—either individually or in combination with other diagnostic modalities—retains critical importance in the early identification and management of PBC-related fibrosis.

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Ethics Committee Approval

The study was performed in accordance with the Declaration of Helsinki, and was approved by the Umraniye Training and Research Hospital, Clinical Research Ethics Committee (Date: 02.11.2023, Decision No. B.10.1.TKH.4.34.H.GP.0.01/412).

Informed Consent

The need for informed consent was waived under the approval of the Local Ethics Committee due to the retrospective design.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author, [N.M.B.].

Author Contributions

Concept – N.M.B. and G.A., Design – N.M.B. and G.A., Supervision – G.A., Data collection and/or processing – N.M.B. and G.A., Analysis and/or interpretation – N.M.B. and G.A., Writing – N.M.B., Critical review- G.A. All authors read and approved the final version of the manuscript.

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