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Biopsy-Based Head-to-Head Comparison of Eight Non-Invasive Fibrosis Scores in Treatment-Naïve Chronic Hepatitis B

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Abstract

Background and Aims

Accurate fibrosis staging is essential for managing chronic hepatitis B (CHB). Although several non-invasive fibrosis scores have been proposed as alternatives to liver biopsy, their comparative performance across fibrosis stages remains uncertain. This study compared eight commonly used non-invasive fibrosis scores for detecting significant, advanced, and severe fibrosis in treatment-naïve patients with CHB.

Materials and Methods

This retrospective study included treatment-naïve patients with CHB who underwent liver biopsy between May 2017 and May 2024. Fibrosis was staged using the Ishak scoring system. APRI, FIB-4, KING, GUCI, AAR, API, INPR, and GPR were evaluated for detecting F ≥ 2, F ≥ 3, and F ≥ 4 fibrosis using receiver operating characteristic (ROC) analysis. Optimal cut-off values were determined using the Youden index. AUROC, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Pairwise AUROC comparisons were performed using DeLong's test.

Results

A total of 268 patients were included. All scores showed poor performance for detecting significant fibrosis (F ≥ 2), with AUROC values below 0.60. Diagnostic accuracy improved for advanced and severe fibrosis. KING achieved the highest AUROC for advanced fibrosis (0.807), followed by FIB-4 (0.797), whereas GPR showed the highest AUROC for severe fibrosis (0.929). DeLong analysis demonstrated no significant differences among the best-performing scores.

Conclusion

None of the evaluated scores demonstrated sufficient accuracy to replace liver biopsy for detecting significant fibrosis. However, FIB-4, KING, and GPR showed good performance for advanced and severe fibrosis and may be useful for initial risk stratification and identifying patients who require further evaluation with liver biopsy.

Introduction

With an estimated 254 million people chronically infected globally and over 6,000 new infections reported every day, hepatitis B virus (HBV) infection remains a serious global health problem [1]. In Turkey, the general incidence of Chronic Hepatitis B (CHB) was documented at 4.57% in 2011, corresponding to around 3.3 million affected individuals. HBV infection remains a leading cause of liver-related morbidity and mortality in the country, contributing to 30–40% of cirrhosis cases and 40–50% of hepatocellular carcinoma (HCC) cases, thereby highlighting its significant public health impact [2].

Parenteral exposure to contaminated blood or bodily fluids, sexual activity, perinatal transmission from an infected mother to her newborn; horizontal spread through close, non-sexual contact. In highly endemic regions, perinatal transmission represents the predominant mode of infection [3–4].

A variety of biochemical, serological, and molecular assays are used in the clinical care of CHB for both diagnosis and monitoring. Nevertheless, definitive staging of hepatic fibrosis and necroinflammatory activity depends on histopathological evaluation via liver biopsy [5]. Despite its diagnostic utility,hemorrhage, pain, bile peritonitis, pneumothorax, hemothorax, bacteremia, and sepsis are among the potential risks of liver biopsy, an invasive procedure.

Due to these limitations, non-invasive serum-based markers have gained prominence in clinical practice. These include direct markers like FibroTest and commonly employed indirect indices such as the Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) and the Fibrosis-4 (FIB-4) score. Additionally, various other non-invasive scores have been developed, including the KING score, AST/ALT ratio (AAR), age-platelet index (API), Gothenburg University Cirrhosis Index (GUCI), INR-platelet ratio (INPR), and GGT-platelet ratio (GPR) [6, 7].

The clinical importance of these non-invasive scores has recently increased in Türkiye following the amendment to the Health Implementation Communiqué (SUT) published in the Official Gazette (No. 32710) on November 2, 2024, which officially recognized APRI and FIB-4 as criteria for initiating antiviral therapy in selected patients with CHB [8]. This regulatory update has further emphasized the need for comparative validation studies evaluating the diagnostic performance of commonly used fibrosis scores in real-world clinical practice.

Although numerous studies have evaluated individual non-invasive fibrosis scores, direct head-to-head comparisons of multiple routinely used indices within the same biopsy-confirmed cohort remain limited. Furthermore, differences in study populations, fibrosis staging systems, and diagnostic thresholds have resulted in inconsistent findings regarding their comparative diagnostic performance. Consequently, the optimal non-invasive score for different stages of liver fibrosis in treatment-naïve patients with CHB remains uncertain.

Therefore, the present study aimed to perform a comprehensive head-to-head comparison of eight widely used non-invasive fibrosis scores (APRI, FIB-4, KING, AAR, API, GUCI, INPR, and GPR) for detecting significant (F ≥ 2), advanced (F ≥ 3), and severe fibrosis (F ≥ 4) in treatment-naïve patients with CHB using liver biopsy as the reference standard. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis. Optimal cut-off values were determined using the Youden index, and sensitivity, specificity, positive predictive value, negative predictive value, and area under the ROC curve (AUROC) with 95% confidence intervals were calculated. Pairwise comparisons of AUROCs were performed using the DeLong test. By identifying the strengths and limitations of each score across different fibrosis stages, we aimed to provide clinically relevant evidence to support the selection of appropriate non-invasive fibrosis assessment tools and facilitate more informed decision-making in routine clinical practice.

Materials and Methods

1. Study Population and Design

The medical records of 268 Chronic Hepatitis B (CHB) patients who were not yet receiving therapy and had a percutaneous liver biopsy performed at our facility between May 1, 2017, and May 1, 2024, were included in this retrospective study. Written informed consent was obtained from all participants included in the study. The study protocol was approved by the Clinical Research Ethics Committee (Date: December 4, 2024; Protocol No: 2024-XXXX-2414_2024.12.04_253). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

The primary inclusion criteria were age 18 years or older and documented HBsAg positivity for a duration exceeding six months.

2. Exclusion Criteria

Patients who showed signs of other chronic liver conditions that can exacerbate hepatic fibrosis were not allowed to participate in the trial. Specific exclusion criteria included:

- Co-infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis D virus (HDV).
- Metabolic dysfunction-associated steatohepatitis (MASH).
- Metabolic or hereditary liver disorders, such as Wilson's disease or hemochromatosis.
- Autoimmune hepatitis and alcoholic hepatitis

3. Calculation of Non-Invasive Fibrosis Scores

Eight distinct non-invasive fibrosis scores were calculated for each patient using the following established formulas. Our local laboratory's reference range was used to determine the maximum value of normal (ULN) for AST and GGT.

- APRI = [AST(U/L)/ASTULN)/PlateletCount(10^9/L)] × 100
- FIB-4 = [Age(years)×AST(U/L)] / [PlateletCount(10^9/L)×√ALT(U/L)]
- KING Score = [Age(years)×AST(U/L)×INR] / Platelet Count (10^9/L)
- GPR = [(GGT(U/L)/GGTULN)/PlateletCount(10^9/L)] × 100
- GUCI = [AST(U/L)×INR×100] / Platelet Count (10^9/L)

• AAR = AST (U/L) / ALT (U/L)

- INPR = INR / Platelet Count (10^9/L)
- API Score: This score was calculated as the sum of points assigned for age and platelet count, as follows (Table 1)

Table 1
API score

Age (years)	Point
< 30	0
30–39	1
40–49	2
50–59	3
60–69	4
≥ 70	5
Platelet count (x10^9/L)	
≥ 340	0
280–339	1
220–279	2
160–219	3
100–159	4
40–99	5
< 40	6

4. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version XX (IBM Corp., Armonk, NY, USA) and R software version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria). The normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean ± standard deviation (SD) or median (minimum–maximum) according to their distribution, whereas categorical variables are presented as frequencies and percentages.

Comparisons of demographic characteristics, laboratory parameters, and non-invasive fibrosis scores between fibrosis groups were performed using the independent-samples t-test or Mann–Whitney U test for continuous variables, as appropriate. Comparisons among three fibrosis-stage groups were performed using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test, followed by appropriate post hoc pairwise comparisons when applicable. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

The diagnostic performance of APRI, FIB-4, KING, AAR, API, GUCI, INPR, and GPR for detecting significant fibrosis (F ≥ 2), advanced fibrosis (F ≥ 3), and severe fibrosis (F ≥ 4) was evaluated using receiver operating characteristic (ROC) curve analysis. Separate ROC analyses were performed for the detection of significant fibrosis (F ≥ 2), advanced fibrosis (F ≥ 3), and severe fibrosis (F ≥ 4). The area under the receiver operating characteristic curve (AUROC) and corresponding 95% confidence intervals (95% CIs) were calculated for each score. Optimal cut-off values were determined using the Youden index, and the corresponding sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Pairwise comparisons of AUROCs between non-invasive fibrosis scores were performed using DeLong's test. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics and Comparison According to Significant Fibrosis

A total of 268 treatment-naïve patients with chronic hepatitis B who underwent liver biopsy between May 2017 and May 2024 were included in the study. According to the Ishak fibrosis staging system, 133 (49.6%) patients had mild fibrosis (F0–1), whereas 135 (50.4%) had significant fibrosis (F ≥ 2). HBeAg positivity was observed in 44 (16.4%) patients.

Patients with significant fibrosis (F ≥ 2) had significantly higher HBV DNA levels, INR, AST, ALT, and GGT values than those with mild fibrosis (all p < 0.05). HBeAg positivity and platelet counts were comparable between the two groups. Among the evaluated non-invasive fibrosis scores, FIB-4, KING, and GPR were significantly higher in patients with significant fibrosis, whereas APRI, GUCI, AAR, API, and INPR did not differ significantly between groups (Table 2).

Table 2
Comparison of Demographic Characteristics, Laboratory Results, and Scores by F ≥ 2 Stage

HBeAg positive n (%)	**All Patients**	**Stage 0–1**	**Stage 2-3-4-5-6**	**p**
	n:268	**n:133**	**n:135**	
	44 (16.4)	**20 (15)**	**24 (17.1)**	**0.545**
HBV DNA (IU/ml) Median	16475	11647	18516	**0.04**
(min-max)	(217-20339911589)	(287-5103159897)	(217-20339911589)	
Platelet count (103 /µl) Mean ± SD	224.6 ± 58.9	225.5 ± 58.4	223.8 ± 59.5	0.817
INR, Mean ± SD	1 ± 0.1	0.98 ± 0.093	1.02 ± 0.11	**0.002**
AST (IU/L), Median	25	25	26	**0.036**
(min-max)	(5-544)	(5-544)	(11–391)	
ALT (IU/L), Median	27.5	26	32	**0.016**
(min-max)	(8-1434)	(9-1434)	(8-468)	
GGT, IU/L, Median	23	20	26.5	**0.008**
(min-max)	(6-408)	(6-166)	(7-408)	
APRI, Median	0.304	0.29	0.32	0.153
(min-max)	(0.01–8.19)	(0.041–8.19)	(0.01–4.96)	
FIB4, Median	0.9	0.84	1.01	**0.02**
(min-max)	(0.22–6.22)	(0.22–3.65)	(0.26–6.22)	
KİNG Score, Median	4.868	4.4	5.21	**0.016**
(min-max)	(0.84–124)	(0.84–34.3)	(0.9–124)	
GPR Score, Median	0.3	0.275	0.32	**0.048**
(min-max)	(0.061-7.8)	(0.064-1)	(0.061-7.8)	
GUCI Score, Median	0.303	0.296	0.319	0.158
(min-max)	(0.01–7.29)	(0.04–7.29)	(0.01–6.2)	
AAR Score, Mean ± SD	0.96 ± 0.36	0.93 ± 0.37	0.98 ± 0.42	0.233
API Score, Mean ± SD	4.29 ± 1.807	4.11 ± 1.66	4.48 ± 1.92	0.088
INPR Score, Median	0.0045	0.00445	0.0045 (0.0023-0.04)	0.324
(min-max)	(0.0022-0.04)	(0.0022–0.0088)		

(HBeAg: Hepatitis B e-Antigen, HBV DNA: Hepatitis B virus DNA, INR: International Normalized Ratio ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, APRI: AST to Platelet Ratio Index, FIB4: Fibrosis-4 score, GPR: GGT to Platelet Ratio, GUCI: Gothenburg University Cirrhosis Index, AAR: AST -to- ALT Ratio, API: Age-Platelet Index, INPR: INR-to-Platelet Ratio)

Comparison of Non-Invasive Fibrosis Scores Across Histological Fibrosis Stages

Patients were subsequently classified into three histological fibrosis stages: mild fibrosis (F0–1), moderate fibrosis (F2–3), and severe fibrosis (F4–6). Significant differences were observed among fibrosis stages for APRI, FIB-4, KING, GPR, GUCI, API, and INPR (all $p < 0.001$), whereas AAR did not differ significantly ($p = 0.687$).

Post hoc analysis demonstrated that APRI, FIB-4, KING, GPR, GUCI, API, and INPR were significantly higher in patients with severe fibrosis (F4–6) than in those with mild (F0–1) or moderate fibrosis (F2–3). However, no statistically significant differences were observed between the mild and moderate fibrosis groups for these scores (Table 3).

Table 3
Comparison of Non-Invasive Fibrosis Scores According to Histological Fibrosis Stage

Parameter	Mild Fibrosis (F 0–1 N:133)	Moderate Fibrosis (F 2–3 N:116)	Severe Fibrosis (F 4-5-6 N:19)	p-value	Post-hoc Comparisons
APRI (median, min-max)	0.29 (0.04–8.19)[a]	0.29 (0.01–2.93)[a]	0.84 (0.23–4.96)[b]	**< 0.001**	**<0.01**
FIB-4 (median, min-max)	0.84 (0.22–3.65)[a]	0.9 (0.26–5.21)[a]	2.14 (1.15–6.22)[b]	**< 0.001**	**<0.01**
KING Score (median, min-max)	4.4 (0.84–34.3)[a]	4.86 (0.9–88.8)[a]	19.02 (1.3–124)[b]	**< 0.001**	**< 0.01**
GPR (median, min-max)	0.27 (0.06-1)[a]	0.29 (0.06–1.65)[a]	0.85 (0.39–7.8)[b]	**< 0.001**	**< 0.01**
GUCI (median, min-max)	0.29 (0.04–7.29)[a]	0.29 (0.01–3.51)[a]	0.89 (0.25–6.2)[b]	**< 0.001**	**< 0.01**
AAR (mean ± SD)	0.93 ± 0.37	0.99 ± 0.43	0.93 ± 0.31	0.687	-
API (mean ± SD)	4.1 ± 1.66[a]	4.16 ± 1.8[a]	6.42 ± 1.5[b]	**< 0.001**	**< 0.01**
INPR (median, min-max)	0.0044 (0.0022–0.0088)[a]	0.0044 (0.0023-0.04)[a]	0.007 (0.0035-0.01)[b]	**< 0.001**	**< 0.01**

(APRI: AST to Platelet Ratio Index, FIB4: Fibrosis-4 score, GPR: Gama-glutamyl transferase to Platelet Ratio, GUCI: Gothenburg University Cirrhosis Index, AAR: Aspartate aminotransferase-to-Alanin aminotransferase Ratio, API: Age-Platelet Index, INPR: INR-to-Platelet Ratio)

Values sharing the same superscript letter are not significantly different, whereas different superscript letters indicate statistically significant differences according to Dunn–Bonferroni post hoc analysis ($p < 0.05$).

Diagnostic Accuracy of Non-Invasive Fibrosis Scores for Significant, Advanced, and Severe Fibrosis

Receiver operating characteristic (ROC) curve analyses were performed to evaluate the diagnostic performance of eight non-invasive fibrosis scores for detecting significant (F ≥ 2), advanced (F ≥ 3), and severe fibrosis (F ≥ 4).

For the detection of significant fibrosis (F ≥ 2), all evaluated scores demonstrated modest diagnostic performance, with AUROC values below 0.60. FIB-4 (AUROC: 0.582), KING (AUROC: 0.585), and GPR (AUROC: 0.573) showed the highest discriminative ability, although overall diagnostic accuracy remained limited.

Diagnostic performance improved substantially for advanced fibrosis (F ≥ 3). KING achieved the highest AUROC (0.807), followed by FIB-4 (0.797), GUCI (0.767), GPR (0.756), and APRI (0.755).

For severe fibrosis (F ≥ 4), GPR demonstrated the highest AUROC (0.929), followed by FIB-4 (0.907), KING (0.883), GUCI (0.868), and APRI (0.859). The optimal cut-off values together with sensitivity, specificity, PPV, and NPV for each score are presented in Table 4.

Table 4
Diagnostic Performance of Eight Non-Invasive Fibrosis Scores for Detecting Significant (F ≥ 2), Advanced (F ≥ 3), and Severe Fibrosis (F ≥ 4)

Score	F ≥ 2 AUROC (95% CI)	Cut-off	Sens (%)	Spec (%)	PPV (%)	NPV (%)	F ≥ 3 AUROC (95% CI)	Cut-off	Sens (%)	Spec (%)	PPV (%)	NPV (%)	F ≥ 4 AUROC (95% CI)	Cut-off	Sens (%)	Spec (%)
APRI	0.550 (0.481–0.620)	0.50	33.3	81.2	64.3	54.5	0.755 (0.678–0.832)	0.50	78.9	69.7	28.9	93.0	0.859 (0.781–0.937)	0.50	100.0	71.1
FIB-4	0.582 (0.514–0.651)	0.84	58.5	60.2	59.8	58.8	0.797 (0.724–0.871)	1.14	78.9	68.9	31.1	95.2	0.907 (0.856–0.958)	1.49	100.0	83.5
KING	0.585 (0.517–0.654)	8.56	23.7	91.7	74.4	54.2	0.807 (0.735–0.879)	5.78	84.2	70.6	33.7	96.4	0.883 (0.812–0.953)	8.56	100.0	76.7
AAR	0.473 (0.404–0.543)	0.91	47.4	57.9	53.3	52.0	0.519 (0.419–0.618)	1.01	57.9	53.5	18.5	88.4	0.513 (0.374–0.651)	1.08	66.7	49.8
API	0.558 (0.490–0.626)	4.50	50.4	60.9	56.7	54.7	0.733 (0.650–0.815)	4.50	68.4	77.6	33.8	92.7	0.843 (0.752–0.933)	5.50	100.0	75.5
GUCI	0.550 (0.482–0.619)	0.57	21.5	92.5	75.0	53.9	0.767 (0.691–0.843)	0.36	78.9	65.8	27.8	93.8	0.868 (0.794–0.942)	0.57	100.0	73.9
INPR	0.535 (0.467–0.603)	0.0057	8.9	97.0	80.0	51.8	0.715 (0.627–0.803)	0.0054	68.4	78.4	32.9	91.8	0.833 (0.742–0.923)	0.0057	100.0	79.4
GPR	0.573 (0.505–0.641)	0.57	20.7	93.4	78.4	54.8	0.756 (0.680–0.833)	0.39	73.7	74.6	32.9	94.0	0.929 (0.881–0.977)	0.39	100.0	73.5

(APRI: AST to Platelet Ratio Index, FIB4: Fibrosis-4 score, GPR: Gama-glutamyl transferase to Platelet Ratio, GUCI: Gothenburg University Cirrhosis Index, AAR: As aminotransferase-to-Alanin aminotransferase Ratio, API: Age-Platelet Index, INPR: INR-to-Platelet Ratio, GPR: Gamma-glutamyl transferase to Platelet Ratio)

Data are presented as the area under the receiver operating characteristic curve (AUROC) with 95% confidence intervals (95% CI). Optimal cut-off values were determined using the Youden index. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each optimal cut-off.

Comparison of Diagnostic Performance

Pairwise comparison of ROC curves using DeLong's test demonstrated no statistically significant differences between the AUROCs of the evaluated fibrosis scores across any fibrosis threshold (all $p > 0.05$). Therefore, although small numerical differences in AUROC values were observed, none of the evaluated scores showed statistically superior diagnostic performance.

Discussion

Accurate non-invasive assessment of liver fibrosis remains a major challenge in the management of chronic hepatitis B [9]. In this biopsy-confirmed cohort of treatment-naïve patients with CHB, we performed a comprehensive head-to-head comparison of eight routinely used non-invasive fibrosis scores across three clinically relevant fibrosis thresholds. The principal findings of this study were threefold. First, all evaluated scores demonstrated limited diagnostic performance for identifying significant fibrosis (F ≥ 2), with AUROC values below 0.70. Second, diagnostic performance improved considerably with increasing fibrosis severity, particularly for advanced (F ≥ 3) and severe fibrosis (F ≥ 4). Third, although KING and GPR achieved the highest AUROC values for advanced (F ≥ 3) and severe fibrosis (F ≥ 4), respectively, pairwise DeLong analysis demonstrated no statistically significant differences among the best-performing scores, indicating comparable diagnostic performance.

The relatively modest diagnostic performance observed for significant fibrosis (F ≥ 2) is consistent with previous studies evaluating serum-based fibrosis indices in CHB [10–11]. Unlike advanced fibrosis or cirrhosis, early fibrotic changes are often associated with limited alterations in routinely measured biochemical and hematological parameters, reducing the discriminatory capacity of indirect fibrosis scores. Consequently, although FIB-4, KING, and GPR showed statistically significant AUROC values, their diagnostic accuracy remained insufficient to support their use as stand-alone diagnostic tools for clinical decision-making.

In contrast, the diagnostic performance of the evaluated scores improved substantially for advanced and severe fibrosis. This finding is biologically plausible because progressive fibrosis is accompanied by more pronounced thrombocytopenia, increasing alterations in transaminase levels, and changes in cholestatic enzymes, resulting in greater separation between fibrosis stages [12–14]. Among the evaluated scores, KING demonstrated the highest AUROC for advanced fibrosis, whereas GPR achieved the highest AUROC for severe fibrosis. However, DeLong analysis demonstrated that these numerical differences were not statistically significant, suggesting that several commonly used non-invasive scores provide similar diagnostic performance in patients with advanced liver fibrosis.

Previous studies have reported variable diagnostic performances for APRI, FIB-4, GPR, and other indirect fibrosis indices in patients with CHB [15–17]. Differences in patient characteristics, antiviral treatment status, fibrosis prevalence, histological scoring systems, and diagnostic cut-off values have likely contributed to the heterogeneity observed across published studies [18, 19].Unlike many previous investigations that evaluated only one or two fibrosis scores, the present study simultaneously compared eight widely used non-invasive indices within the same biopsy-confirmed treatment-naïve cohort using identical fibrosis definitions and statistical methodology, allowing a more robust head-to-head assessment of their relative performance.

Our findings are also relevant in light of the recent revision of the Turkish Health Implementation Communiqué (SUT), which incorporated APRI and FIB-4 into treatment decision algorithms for selected patients with CHB. Although these scores demonstrated acceptable performance for advanced fibrosis, their limited accuracy for significant fibrosis indicates that they should be interpreted together with clinical, laboratory, and imaging findings rather than used in isolation.

From a clinical perspective, our findings suggest that routinely available non-invasive fibrosis scores may be useful as first-line assessment tools, particularly for excluding advanced fibrosis and prioritizing patients for further evaluation. However, because no individual score consistently outperformed the others and diagnostic performance remained limited for significant fibrosis, liver biopsy and elastography continue to play an essential role when accurate staging is required. Rather than replacing liver biopsy, these inexpensive and widely available indices should be considered complementary tools within a sequential diagnostic strategy.

This study has several strengths. It included a relatively large biopsy-confirmed cohort of treatment-naïve patients with CHB, evaluated eight widely used non-invasive fibrosis scores within the same study population, and compared their diagnostic performance across three clinically relevant fibrosis thresholds using ROC and DeLong analyses. These design characteristics minimized methodological heterogeneity and enabled direct comparison between commonly used fibrosis indices. Nevertheless, several limitations should be acknowledged. First, the retrospective single-center design may limit generalizability. Second, the number of patients with severe fibrosis (F4–6) was relatively small, which may have reduced the precision of some diagnostic estimates. Third, transient elastography was not available for comparison. Future prospective multicenter studies with external validation cohorts and direct comparisons with transient elastography are warranted to further establish the clinical utility of these non-invasive fibrosis scores.

Conclusion

In conclusion, none of the evaluated non-invasive fibrosis scores demonstrated sufficient diagnostic accuracy to replace liver biopsy for identifying significant fibrosis in treatment-naïve patients with chronic hepatitis B. However, several readily available indices, particularly FIB-4, KING, and GPR, showed good performance for detecting advanced fibrosis, with no statistically significant differences between the best-performing scores. These findings support the use of non-invasive fibrosis scores as complementary tools for initial risk stratification rather than as stand-alone diagnostic methods. Further prospective multicenter studies are needed to validate these findings and optimize non-invasive fibrosis assessment in patients with chronic hepatitis B.

Declarations

Ethics Approval Statement

The study protocol was approved by the **Yozgat Bozok University Clinical Research Ethics Committee** (Date: December 4, 2024; Protocol No: 2024-GOKAEK-2414_2024.12.04_253). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author.

Consent for publication

Not Applicable.

Informed Consent

Written informed consent was obtained from all participants included in the study.

Declaration of Interests

The authors have no conflicts of interest to declare.

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Author Contributions

Concept – S.Z.D.Y,H.E. Design – S.Z.D.Y.Supervision – S.Z.D.Y,H.E. Resources – S.Z.D.Y,H.E.; Materials – S.Z.D.Y,H.E.; Data Collection and/or Processing – S.Z.D.Y,H.E.; Analysis and/or Interpretation – S.Z.,H..E; Literature Search – S.Z.D.Y,H.E.; Writing Manuscript – S.Z.D.Y,H.E.; Critical Review – S.Z.D.Y,H.E

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