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ORIGINAL RESEARCH

Discriminative performance of non-invasive scoring systems for VCTE-defined steatosis and fibrosis in patients with psoriasis

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Highlights & Insights

- **Scientific Gap:** The optimal non-invasive screening strategy for VCTE-defined hepatic steatosis and fibrosis in patients with psoriasis remains uncertain.
- **Key Finding:** Fibrosis scores showed limited discrimination, although SAFE and BARD had high negative predictive values. FLI performed best for steatosis, followed by HSI and MAFLD-S.
- **Clinical Impact:** These scores may support preliminary triage, especially where VCTE is unavailable; low fibrosis scores can help rule out significant fibrosis, whereas elevated results require elastographic confirmation.

ABSTRACT

Background and Aim: Metabolic dysfunction-associated steatotic liver disease (MASLD) is more prevalent in patients with psoriasis. Reliable non-invasive tools are needed to evaluate hepatic steatosis and to identify patients at risk for significant liver fibrosis. This study aimed to assess the discriminative performance of commonly used non-invasive scoring systems for identifying patients with vibration-controlled transient elastography (VCTE)-defined significant liver fibrosis and hepatic steatosis in patients with psoriasis.

Materials and Methods: A total of 113 patients with psoriasis were prospectively enrolled. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) were assessed using VCTE. Significant fibrosis (F2–F4) was defined as LSM ≥8 kPa, and significant steatosis (S2–S3) as CAP ≥259 dB/m. The discriminative performance of non-invasive fibrosis and steatosis scores was evaluated using area under the receiver operating characteristic (AUROC) curves.

Results: Of the 113 patients, 76 (67%) were diagnosed with MASLD following VCTE assessment. The body mass index, aspartate aminotransferase–alanine aminotransferase ratio, and diabetes (BARD) score (AUROC=0.692) showed the highest performance in identifying significant fibrosis, while FIB-4, aspartate aminotransferase to platelet ratio index, non-alcoholic fatty liver disease fibrosis score (NFS), and steatosis-associated fibrosis estimator (SAFE) demonstrated lower predictive accuracy. Among patients with MASLD, the SAFE score (AUROC=0.776), followed by the BARD score (AUROC=0.716), yielded the highest discriminative performance. The SAFE score showed the highest negative predictive value (95%) for ruling out significant fibrosis in MASLD patients. For detecting significant steatosis, the fatty liver index (FLI) score (AUROC=0.867) provided the highest performance, while hepatic steatosis index (HSI) (AUROC=0.813) and metabolic dysfunction–associated fatty liver disease screening score (MAFLD-S) (AUROC=0.833) also demonstrated good discriminative ability.

Conclusion: In patients with psoriasis, commonly used non-invasive fibrosis scores showed limited discrimination for VCTE-defined significant fibrosis, but they may have value as rule-out tools in low-prevalence settings. In contrast, FLI, HSI, and MAFLD-S showed good discrimination for VCTE-defined significant hepatic steatosis.

Keywords: Metabolic dysfunction-associated steatotic liver disease; non-invasive scoring systems; psoriasis.

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease with a global prevalence ranging from 0.09% to 5.1%. It is characterized by well-demarcated, erythematous, scaly plaques typically located on the trunk, scalp, and extremities.[1,2] In recent years, psoriasis has been recognized not merely as a cutaneous disorder but as a systemic inflammatory condition associated with increased mortality and a substantial burden of comorbidities. Notably, metabolic syndrome, type 2 diabetes, obesity, dyslipidemia, and hypertension are frequently observed in conjunction with psoriasis.[3]

Metabolic dysfunction–associated steatotic liver disease (MASLD) is observed 1.5–3 times more frequently in individuals with psoriasis compared with the general population. In the literature, the reported prevalence of MASLD in patients with psoriasis ranges from 17% to 60%, and this patient group has also been shown to have a markedly higher prevalence of advanced liver fibrosis.[4] This association cannot be explained solely by shared risk factors; it has been proposed that psoriasis may increase the risk of developing hepatic steatosis and fibrosis independently of obesity.[5] Among the key mechanisms underlying this pathophysiological process are the effects of tumor necrosis factor-alpha, interleukin-6, and interleukin-17 released from psoriatic skin, which promote hepatic inflammation and insulin resistance, leading to increased triglyceride accumulation within hepatocytes.[6–8]

The management of psoriasis requires a personalized and holistic approach, taking into consideration the disease severity, phenotype, comorbidities, and the needs of the individual. Accordingly, systemic therapies are frequently employed, particularly in moderate-to-severe cases. Methotrexate (MTX) is one of the conventional systemic agents being used for the treatment of psoriasis and psoriatic arthritis. It may exert hepatotoxic effects, including elevations in liver enzymes and potential liver fibrosis with long-term use.[9] In patients with risk factors such as obesity, diabetes, and excessive alcohol consumption, this risk becomes even more pronounced. Current guidelines recommend screening for MASLD before initiating treatment in patients with moderate-to-severe psoriasis and advise a more cautious approach when considering MTX therapy.[10]

Over the past two decades, considerable effort has been devoted to developing accessible and cost-effective non-invasive diagnostic tools as alternatives to liver biopsy in MASLD. While ultrasonography remains the first-line method for assessing steatosis, the use of non-invasive scoring systems has been increasingly adopted in large population studies. Given that the stage of fibrosis is the most critical determinant of mortality in MASLD, the non-invasive detection of advanced fibrosis holds substantial clinical importance for patient management.[11] For this purpose, vibration-controlled transient elastography (VCTE) has become the most widely used and clinically useful non-invasive modality for liver fibrosis and steatosis assessment, as the best alternative to the gold standard liver biopsy.[12] In addition to radiologic methods, several clinical scoring systems – such as the Fibrosis-4 (FIB-4), aspartate aminotransferase to platelet ratio index (APRI), non-alcoholic fatty liver disease fibrosis score (NFS), body mass index, aspartate aminotransferase–alanine aminotransferase ratio, and diabetes (BARD), and the steatosis-associated fibrosis estimator (SAFE) score – have been developed and validated in various studies to assess fibrosis risk in MASLD.[13–17] Similar to non-invasive fibrosis scores, non-invasive steatosis scoring systems such as the fatty liver index (FLI), hepatic steatosis index (HSI), and the metabolic dysfunction–associated fatty liver disease screening score (MAFLD-S), which are derived from combinations of clinical features and routine laboratory parameters, have also been developed as practical tools for steatosis quantification.[18–20]

Since the data on optimal screening method for patients with psoriasis for liver fibrosis is uncertain, this study aimed to evaluate the discriminative ability of commonly used serum-based non-invasive fibrosis and steatosis scores against VCTE-defined fibrosis and steatosis in patients with psoriasis, and to explore the potential utility for identifying patients who may warrant further liver assessment.

Materials and Methods

Study Design, Patient Selection, and Data Collection

In this cross-sectional study, 117 patients diagnosed with psoriasis who presented to a tertiary dermatology outpatient clinic at Marmara University between January 2024 and December 2024 were prospectively evaluated for enrollment to the present study. Consecutive patients with psoriasis attending the dermatology clinic were evaluated, and VCTE was performed as part of the liver assessment rather than only in patients with suspected liver disease. Patients older than 18 years with a clinical diagnosis of psoriasis confirmed by an expert dermatologist were included. Patients were excluded if they had unreliable VCTE results, viral hepatitis seropositivity, previously known liver disease, significant alcohol consumption (for women >20 g/day, for men >30 g/day), or missing data required for the calculation of non-invasive scores. As a result, the final analyses were conducted with 113 patients with reliable VCTE measurement and available non-invasive scores.

Demographic and clinical data were collected through medical history and patient interviews. Body mass index (BMI) was used to classify participants as normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥30.0 kg/m^2). Furthermore, waist and hip circumferences were measured using standard techniques. Current alcohol and tobacco use were recorded, and patients were categorized into two groups based on MTX use. MTX use and cumulative dose were determined from patient records and monitoring charts. For patients receiving biologic therapy, treatment type and duration were documented. Comorbidities, including hypertension, type 2 diabetes, and dyslipidemia, were assessed, and MASLD was defined according to international consensus criteria based on hepatic steatosis plus the presence of metabolic risk factors assessed in routine clinical practice. Clinical and laboratory data were obtained within ±3 months of the VCTE assessment. Serum parameters (complete blood count, liver function tests, lipid profile, C-reactive protein, etc.) were measured after a 12-h fasting period. Viral hepatitis screening was

Table 1. Demographic, clinical, and laboratory findings

	Whole cohort (n=113)		Whole cohort (n=113)
Age, mean±SD, years	46.9±13.4	Biologics, n (%)	
Sex, n (%)		Risankizumab	20 (17.7)
Female	49 (43.4)	Ustekinumab	17 (15.0)
Male	64 (56.6)	Ixekizumab	17 (15.0)
Height, median (min-max), cm	169 (150–192)	Guselkumab	9 (8.0)
Weight, median (min-max), kg	79 (44–127)	Adalimumab	7 (6.2)
BMI, median (min-max), kg/m^2	28.7 (18.6–45.9)	Infliximab	6 (5.3)
Waist circumference, median (min-max), cm	99 (63–136)	Secukinumab	5 (4.4)
Hip circumference, median (min-max), cm	109 (50–153)	Certolizumab	4 (3.5)
Alcohol use, n (%)	33 (29.2)	Etanercept	1 (0.9)
Smoking, n (%)	70 (62.0)	AST, median (min-max), IU/L	22 (12–80)
MASLD, n (%)	76 (67.0)	ALT, median (min-max), IU/L	20 (6–142)
Comorbidities, n (%)		ALP, median (min-max), IU/L	69 (18–156)
Diabetes mellitus	16 (14.2)	GGT, median (min-max), IU/L	23 (7–168)
Hypertension	16 (14.2)	BUN, median (min-max), mg/dL	13 (7–23)
Dyslipidemia	23 (20.4)	Creatinine, median (min-max), mg/dL	0.8 (0.2–1.5)
Chronic kidney disease	9 (8.0)	Total bilirubin, median (min-max), mg/dL	0.6 (0.2–1.6)
Coronary artery disease	2 (1.8)	Total protein, median (min-max), g/dL	7.2 (5.7–8.5)
Congestive heart failure	0 (0.0)	Albumin, median (min-max), g/dL	4.4 (3.6–5.2)
COPD-Asthma	3 (2.7)	White blood cell count, median (min-max), /µL	8100 (5300–16000)
Malignancy	0 (0.0)	Hemoglobin, median (min-max), g/dL	14.4 (8.7–17.1)
MTX, n (%)	68 (60.2)	Platelets, median (min-max), ×1000/mm^3	258 (155–410)
Dose, median (min-max), mg	15 (5–20)	CRP, median (min-max), mg/L	2.9 (0.1–41.0)
Duration, median (min-max), months	12 (1–120)	HDL cholesterol, median (min-max), mg/dL	48 (26–172)
Cumulative dose, median (min-max), g	0.7 (0.1–7.2)	LDL cholesterol, median (min-max), mg/dL	126 (40–192)
		Total cholesterol, median (min-max), mg/dL	208 (123–301)
		Triglycerides, median (min-max), mg/dL	133 (45–637)

µL: Microliter; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BMI: Body mass index; BUN: Blood urea nitrogen; cm: Centimeter; COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; dL: Deciliter; g: Gram; GGT: Gamma-glutamyl transferase; HDL: High-density lipoprotein; IU: International unit; kg: Kilogram; kg/m^2: Kilogram per square meter; L: Liter; LDL: Low-density lipoprotein; mm^3: Cubic millimeter; MASLD: Metabolic dysfunction-associated steatotic liver disease; mg: Milligram; mL: Milliliter; MTX: Methotrexate; SD: Standard deviation.

performed for all participants using anti-hepatitis C virus, anti-hepatitis B core, and hepatitis B surface antigen assays.

VCTE Measurements

Liver stiffness measurement (LSM) and the controlled attenuation parameter (CAP) were obtained using a FibroScan 530 Compact device equipped with M and XL probes, performed by a physician trained and certified by the manufacturer.[21] All patients were instructed to fast for at least 3 h before the examination, in accordance with the manufacturer's recommendations. Probe selection was performed using the automatic probe selection tool integrated into the device software. For the examination, patients were placed in the supine position, and the probe was positioned over the right lobe of the liver in the 9th–11th intercostal spaces. Reliable VCTE measurements were defined as those with at least 10 valid acquisitions and an interquartile range (IQR)-to-median ratio ≤30%.[22]

CAP represents the mean estimation of ultrasound attenuation at 3.5 MHz and is expressed in decibel-meter (dB/m). LSM represents the mean estimation of stiffness (Young's modulus) at a shear wave frequency of 50 Hz and is expressed in kilopascal (kPa).[23] Patients with LSM values <8.0 kPa were considered to have no or mild liver fibrosis (F0–F1), while those with LSM values ≥8.0 kPa were classified as having significant fibrosis (F2–F4).[24] The presence of significant hepatic steatosis (S2–S3) was defined as CAP ≥259 dB/m.[25]

Calculation of Non-invasive Scores

Five non-invasive fibrosis scores, FIB-4, APRI, NFS, BARD, and SAFE, and three non-invasive steatosis scores, FLI, HSI, and MAFLD-S, were calculated. FIB-4, APRI, NFS, SAFE, FLI, HSI, and MAFLD-S were computed using their original formulas.[13–15,17–20] The BARD score was calculated based on the scoring of three variables.[16] FIB-4, APRI, NFS, BARD, and SAFE scores were compared with LSM (kPa), whereas FLI, HSI, and MAFLD-S results were compared with CAP (dB/m) values.

Determination of Cut-off Values

Receiver operating characteristic (ROC) curves were constructed to assess the overall accuracy of the non-invasive scoring systems and to determine optimal cut-off points. The Youden index was used to establish the optimal threshold for non-invasive scores in identifying significant fibrosis and significant steatosis. The optimal cut-off values in this study are mainly study-derived exploratory cut-off values using the Youden index. The literature established cut-off values were derived from their original publications.[13–20]

Statistical Analysis

Continuous variables were summarized as mean ± SD (normally distributed) or median (range) (non-normally distributed), and categorical variables as n (%). Between-group comparisons used the independent Student's t-test for normally distributed continuous variables, the Mann–Whitney U test for non-normally distributed continuous variables, and the χ^2 test for categorical variables. A $p<0.05$ was considered statistically significant.

The diagnostic performance of non-invasive tests was evaluated using ROC curves. The area under the ROC curve (AUROC) was used as an indicator for comparing test accuracy. In addition, true positive, true negative, false positive, and false negative values were calculated by comparing non-invasive scores with VCTE results at various cut-off points. Metrics such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each cut-off value using MedCalc software (version 23.1.3; MedCalc Software Ltd., Ostend, Belgium). All statistical analyses were performed using Statistical Package for the Social Sciences software (version 27.0; IBM Corp., Armonk, New York, USA).

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Marmara University School of Medicine Clinical Research Ethics Committee (Approval Date: 12 January 2024; Approval No. 09.2024.115). Written informed consent was obtained from all participants.

Results

Patient Characteristics and VCTE Findings

Seventy-six patients (67%) met the diagnostic criteria for MASLD. The cohort consisted of 56.6% males, with a mean age of 46.9±13.4 years. Based on BMI distribution, 37 patients (32.7%) were obese, 49 (43.4%) were overweight, and 27 (23.9%) had normal weight. Regarding metabolic comorbidities, diabetes mellitus was present in 16 patients (14.2%), hypertension in 16 patients (14.2%), and dyslipidemia in 23 patients (20.4%). Elevated alanine aminotransferase (>45 IU/L) was observed in 10 of 113 patients (8.8%). In the entire cohort, the median MTX dose was 15 (5–20) mg, duration 12 (1–120) months, and cumulative dose 0.7 (0.1–7.2) g. Eighty-six patients (76%) were receiving biologic therapy, with risankizumab being the most commonly used agent (17.7%) (Table 1).

Table 2. Serum-based non-invasive scores and vibration-controlled transient elastography findings

	Whole cohort (n=113)
Steatosis scores	
FLI, median (min-max)	62 (1–100)
HSI, mean±SD	38.5±6.8
MAFLD-S, median (min-max)	0.3 (-12.4–6.7)
Fibrosis scores	
FIB-4, median (min-max)	0.8 (0.2–2.5)
APRI, median (min-max)	0.2 (0.1–0.9)
NFS, mean±SD	-2.4±1.3
BARD, median (min-max)	2 (0–4)
SAFE, median (min-max)	-42.3 (–260.6–360.1)
VCTE	
LSM, median (min-max), kPa	5.3 (2.5–18.0)
CAP, mean±SD, dB/m	268.0±57.4
IQR/M, mean±SD, %	13.1±4.4

APRI: Aspartate aminotransferase-to-platelet ratio index; BARD: Body mass index; aspartate aminotransferase-alanine aminotransferase ratio; and diabetes; CAP: Controlled attenuation parameter; dB/m: Decibel-meter; FIB-4: Fibrosis-4 score; FLI: Fatty liver index; HSI: Hepatic steatosis index; IQR/M: Interquartile range/median; kPa: Kilopascal; LSM: Liver stiffness measurement; MAFLD-S: Metabolic dysfunction-associated fatty liver disease screening score; NFS: Non-alcoholic fatty liver disease fibrosis score; SAFE: Steatosis-associated fibrosis estimator; VCTE: Vibration-controlled transient elastography.

Patients were divided into two groups based on MTX exposure: 68 patients (60.2%) were using MTX, while 45 (39.8%) were not. No significant differences were observed between the groups in terms of demographic characteristics (age, sex) or metabolic risk factors (type 2 diabetes, dyslipidemia, hypertension, BMI, and MASLD). There were also no statistically significant differences in liver enzyme levels between MTX users and non-users.

Among the 113 patients with reliable VCTE measurements, the mean CAP was 268.0 ± 57.4 dB/m, the median LSM was 5.3 (2.5–18.0) kPa, and the mean IQR/M was 13.1 ± 4.4%. MTX users exhibited a higher median LSM compared with non-users; however, the difference was not statistically significant (p=0.286). Based on LSM values, 12 patients (10.5%) exhibited significant fibrosis (F2–F4), and 65 patients (57%) had significant steatosis (S2–S3).

Table 3. Performance of serum-based non-invasive fibrosis scoring systems with exploratory cut-off values in detecting significant fibrosis

	FIB-4	APRI	NFS	BARD	SAFE
A. Whole cohort (n=113)					
Optimal cut-off	**0.86**	**0.25**	**-1.88**	**2.50**	**-10.83**
Sensitivity, (%)	41.7	41.7	50.0	66.7	66.7
Specificity, (%)	56.4	65.3	65.3	62.4	64.3
NPV, (%)	89.0	90.4	91.7	94.0	94.2
PPV, (%)	10.2	12.5	14.6	17.4	18.2
FPR, (%)	44/101 (43.6)	35/101 (34.7)	35/101 (34.7)	38/101 (37.6)	35/101 (34.7)
FNR, (%)	7/12 (58.3)	7/12 (58.3)	6/12 (50.0)	4/12 (33.3)	4/12 (33.3)
AUROC (95% CI)	0.535 (0.395–0.675)	0.609 (0.447–0.772)	0.631 (0.482–0.780)	0.692 (0.536–0.849)	0.678 (0.504–0.853)
B. MASLD subgroup (n=76)					
Optimal cut-off	**1.13**	**0.35**	**-1.60**	**2.50**	**-10.51**
Sensitivity, (%)	33.3	33.3	55.6	77.8	77.8
Specificity, (%)	73.1	86.6	68.7	58.2	65.7
NPV, (%)	88.9	90.6	92.0	95.1	95.7
PPV, (%)	13.6	25.0	19.2	20.0	23.3
FPR, (%)	19/67 (28.4)	9/67 (13.4)	21/67 (31.3)	28/67 (41.8)	23/67 (34.3)
FNR, (%)	6/9 (66.7)	6/9 (66.7)	4/9 (44.4)	2/9 (22.2)	2/9 (22.2)
AUROC (95% CI)	0.551 (0.380–0.721)	0.588 (0.388–0.788)	0.653 (0.535–0.897)	0.716 (0.535–0.897)	0.776 (0.635–0.917)
C. Non-MASLD subgroup (n=37)					
Optimal cut-off	**0.67**	**0.25**	**-2.76**	**2.50**	**-57.83**
Sensitivity, (%)	66.7	66.7	66.7	33.3	33.3
Specificity, (%)	47.0	67.7	61.8	70.6	64.7
NPV, (%)	94.1	95.8	95.5	92.3	91.7
PPV, (%)	10.0	15.4	13.3	9.1	7.7
FPR, (%)	18/34 (52.9)	11/34 (32.4)	13/34 (38.2)	10/34 (29.4)	12/34 (35.3)
FNR, (%)	1/3 (33.3)	1/3 (33.3)	1/3 (33.3)	2/3 (66.7)	2/3 (66.7)
AUROC (95% CI)	0.471 (0.251–0.690)	0.672 (0.414–0.930)	0.549 (0.347–0.751)	0.588 (0.303–0.873)	0.353 (0.067–0.639)
D. MTX user subgroup (n=68)					
Optimal cut-off	**0.77**	**0.35**	**-1.60**	**2.50**	**23.40**
Sensitivity, (%)	50.0	16.7	50.0	83.3	66.7
Specificity, (%)	46.8	87.1	74.2	59.7	72.6
NPV, (%)	90.6	91.5	93.9	97.4	95.7
PPV, (%)	8.3	11.1	15.8	16.7	19.1
FPR, (%)	33/62 (53.2)	8/62 (12.9)	16/62 (25.8)	25/62 (40.3)	17/62 (27.4)
FNR, (%)	3/6 (50.0)	5/6 (83.3)	3/6 (50.0)	1/6 (16.7)	2/6 (33.3)
AUROC (95% CI)	0.492 (0.288–0.695)	0.481 (0.271–0.692)	0.684 (0.482–0.887)	0.801 (0.623–0.979)	0.675 (0.418–0.931)
E. MTX non-user subgroup (n=45)					
Optimal cut-off	**0.86**	**0.25**	**-1.92**	**2.50**	**-11.83**
Sensitivity, (%)	66.7	66.7	50.0	50.0	66.7
Specificity, (%)	56.4	64.1	61.5	66.7	64.1
NPV, (%)	91.7	92.6	88.9	89.7	92.6
PPV, (%)	19.1	22.2	16.7	18.8	22.2
FPR, (%)	17/39 (43.6)	14/39 (35.9)	15/39 (38.5)	13/39 (33.3)	14/39 (35.9)
FNR, (%)	2/6 (33.3)	2/6 (33.3)	3/6 (50.0)	3/6 (50.0)	2/6 (33.3)
AUROC (95% CI)	0.577 (0.387–0.767)	0.735 (0.522–0.948)	0.551 (0.325–0.777)	0.603 (0.375–0.830)	0.667 (0.425–0.909)

APRI: Aspartate aminotransferase-to-platelet ratio index; AUROC: Area under the receiver operating characteristic curve; BARD: Body mass index; aspartate aminotransferase–alanine aminotransferase ratio; and diabetes; CI: Confidence interval; FIB-4: Fibrosis-4 score; FNR: False negative rate; FPR: False positive rate; MASLD: Metabolic dysfunction-associated steatotic liver disease; MTX: Methotrexate; NFS: Non-alcoholic fatty liver disease fibrosis score; NPV: Negative predictive value; PPV: Positive predictive value; SAFE: Steatosis-associated fibrosis estimator.

In the overall cohort, the median FIB-4 was 0.8 (0.2–2.5), median APRI was 0.2 (0.1–0.9), mean NFS was –2.4±1.3, median BARD was 2 (0–4), and median SAFE was -42.3 (-260.6–360.1). For steatosis scores, the median FLI was 62 (1–100), mean HSI 38.5±6.8, and median MAFLD-S 0.3 (-12.4–6.7) (Table 2).

Comparison of Non-invasive Fibrosis and Steatosis Scores with Exploratory Cut-off Values

In the ROC analyses in the entire cohort, the BARD score showed the highest AUROC among the evaluated scores for identifying significant fibrosis, with an AUROC of 0.692 (95% confidence interval [CI], 0.536–0.849). The performance of the other non-invasive tests was as follows: FIB-4 0.535 (95% CI, 0.395–0.675), APRI 0.609 (95% CI, 0.447–0.772), NFS 0.631 (95% CI, 0.482–0.780), and SAFE 0.678 (95% CI, 0.504–0.853). The BARD and SAFE scores showed 66.7% sensitivity and 62.4% and 64.3% specificity, respectively, for detecting significant fibrosis, while the SAFE score with an optimal cut-off of –10.83 achieved the highest NPV (94.2%) among all tests (Table 3).

In the analyses performed to predict significant steatosis (S2–S3), FLI demonstrated the highest discriminative performance in the entire cohort with an AUROC of 0.867 (95% CI, 0.799–0.935), while the HSI and MAFLD-S scores showed good discriminatory ability with AUROCs of 0.813 (95% CI, 0.732–0.894) and 0.833 (95% CI, 0.759–0.907), respectively. In the MASLD subgroup, FLI also showed the highest discriminative performance with an AUROC of 0.769, followed by the MAFLD-S and HSI scores, with AUROCs of 0.755 and 0.706, respectively (Table 4).

In exploratory subgroup analyses, we tested the performance of each non-invasive scoring system across MASLD and MTX strata. In the MASLD subgroup (n=76), when evaluating non-invasive tests for identifying significant fibrosis, the SAFE score demonstrated the highest discriminative performance with an AUROC of 0.776, followed by the BARD score with an AUROC of 0.716. The FIB-4, APRI, and NFS scores showed poor performance in the MASLD subgroup. The sensitivities of the SAFE and BARD scores were above 75%, and their specificities were 65.7% and 58.2%, respectively. The SAFE score, with an optimal cut-off of -10.51, also provided the highest NPV (95.7%) in this subgroup. Among patients without MASLD (n=37), the APRI score showed the highest discriminative performance for identifying significant fibrosis, with an AUROC of 0.672, whereas the other scores exhibited low performance. In this group, the APRI score, with an optimal cut-off of 0.25, yielded an NPV of 95.8%.

In the MTX-treated group (n=68), the BARD score showed the highest AUROC among the evaluated scores for detecting significant fibrosis, with a value of 0.801. The AUROC values the other scores were as follows: FIB-4 0.492, APRI 0.481, NFS 0.684, and SAFE 0.675. In this group, the BARD score achieved a NPV of 97.4% with an optimal cut-off of 2.50. In the group not treated with MTX (n=45), the APRI score showed the highest discriminative performance for significant fibrosis, providing an AUROC value of 0.735 and a NPV of 92.6% at the optimal cut-off of 0.25 (Table 3 and Fig. 1).

In patients using MTX, FLI exhibited the highest performance for detecting significant steatosis, with an AUROC of 0.905, while the HSI and MAFLD-S scores showed AUROCs of 0.823 and 0.844, respectively. Similarly, among patients not using MTX, FLI, HSI, and MAFLD-S demonstrated strong discriminatory ability for detecting significant steatosis, with AUROCs of 0.866, 0.841, and 0.856, respectively (Table 4 and Fig. 2).

Comparison of Non-invasive Fibrosis and Steatosis Scores with Literature Established Cut-off Values

When diagnostic performance was evaluated using established cut-off values, the NPVs were notably high and demonstrated consistency with the results obtained from study-derived exploratory thresholds (Supplementary Table 1). Due to the absence of patients categorized into the "rule-in" zone according to established cut-offs in our cohort, sensitivity and NPV values for FIB-4, APRI, and NFS could not be calculated (Supplementary Table 2, 3). Regarding steatosis scores, established cut-off values yielded higher sensitivity rates (reaching 100% for HSI in the whole cohort) compared to exploratory thresholds, while maintaining high NPVs, albeit with a relatively lower specificity (Supplementary Table 4).

Discussion

In the present study, we evaluated the diagnostic performance of commonly used non-invasive fibrosis and steatosis scores in patients with psoriasis using VCTE as the reference standard. Our findings indicate that, among fibrosis scores, BARD and SAFE scores demonstrated the highest discriminative performance for identifying significant liver fibrosis in the entire cohort and in the MASLD subgroup. In patients without MASLD, APRI score demonstrated the highest discriminative performance. Among MTX users, the BARD score again yielded the highest discriminative performance, whereas in MTX non-users, APRI demonstrated the highest discriminatory ability. These findings likely reflect the populations in which these scores were originally developed, with SAFE and BARD being MASLD-specific tools and APRI having broader applicability across chronic liver disease.

Although MTX exposure has the potential to induce liver fibrosis, we hypothesized that MTX exposure might influence the discriminative performance of the fibrosis scores. However, the limited number of patients with significant fibrosis in our cohort likely reduced our ability to detect such effects. Importantly, no significant differences in liver enzymes or fibrosis frequency were observed between MTX users and non-users.

Regarding significant steatosis prediction, FLI demonstrated the highest discriminative performance across the entire cohort and all subgroups, including MASLD patients and those with or without MTX exposure. The HSI and MAFLD-S scores also showed good discriminative ability, although consistently inferior to FLI. This study is in line with previous studies that have validated FLI and HSI in diverse populations and extends their applicability to patients with psoriasis.

Overall, non-invasive fibrosis scores showed modest diagnostic performance in this population, with AUROC values generally below 0.7. Nevertheless, BARD and SAFE scores outperformed other scoring systems in detecting significant fibrosis, consistent with

Table 4. Performance of serum-based non-invasive steatosis scoring systems with exploratory cut-off values in detecting significant steatosis

	FLI	HSI	MAFLD-S
A. Whole cohort (n=113)			
Optimal cut-off	**50.50**	**36.31**	**-0.41**
Sensitivity, (%)	86.2	78.5	80.0
Specificity, (%)	77.1	68.7	68.7
NPV, (%)	80.4	70.2	71.7
PPV, (%)	83.5	77.3	77.6
FPR, (%)	11/48 (22.9)	15/48 (31.2)	15/48 (31.2)
FNR, (%)	9/65 (13.8)	14/65 (21.5)	13/65 (20.0)
AUROC (95% CI)	0.867 (0.799–0.935)	0.813 (0.732–0.894)	0.833 (0.759–0.907)
B. MASLD subgroup (n=76)			
Optimal cut-off	**70.50**	**37.71**	**0.03**
Sensitivity, (%)	66.2	72.3	73.9
Specificity, (%)	81.8	72.7	72.7
NPV, (%)	29.0	30.8	32.0
PPV, (%)	95.6	94.0	94.1
FPR, (%)	2/11 (18.2)	3/11 (27.3)	3/11 (27.3)
FNR, (%)	22/65 (33.8)	18/65 (27.7)	17/65 (26.2)
AUROC (95% CI)	0.769 (0.617–0.920)	0.706 (0.516–0.896)	0.755 (0.587–0.924)
C. MTX user subgroup (n=68)			
Optimal cut-off	**50.50**	**36.36**	**-0.41**
Sensitivity, (%)	84.8	76.1	78.3
Specificity, (%)	86.4	77.3	72.7
NPV, (%)	73.1	60.7	61.5
PPV, (%)	92.9	87.5	85.7
FPR, (%)	3/22 (13.6)	5/22 (22.7)	6/22 (27.3)
FNR, (%)	7/46 (15.2)	11/46 (23.9)	10/46 (21.7)
AUROC (95% CI)	0.905 (0.833–0.977)	0.823 (0.725–0.921)	0.844 (0.753–0.935)
D. MTX non-user subgroup (n=45)			
Optimal cut-off	**58.50**	**39.90**	**0.63**
Sensitivity, (%)	89.5	84.2	84.2
Specificity, (%)	76.9	92.3	84.6
NPV, (%)	90.9	88.9	88.0
PPV, (%)	73.9	88.9	80.0
FPR, (%)	6/26 (23.1)	2/26 (7.7)	4/26 (15.4)
FNR, (%)	2/19 (10.5)	3/19 (15.8)	3/19 (15.8)
AUROC (95% CI)	0.866 (0.755–0.978)	0.841 (0.709–0.973)	0.856 (0.744–0.969)

AUROC: Area under the receiver operating characteristic curve; CI: Confidence interval; FLI: Fatty liver index; FNR: False negative rate; FPR: False positive rate; HSI: Hepatic steatosis index; MAFLD-S: Metabolic dysfunction–associated fatty liver disease screening score; MASLD: Metabolic dysfunction-associated steatotic liver disease; MTX: Methotrexate; NPV: Negative predictive value; PPV: Positive predictive value.

prior reports demonstrating their limited but clinically useful accuracy.[13–17] In a biopsy-proven MASLD cohort, Ruffillo et al.[26] demonstrated that both NFS and BARD scores had only modest accuracy for identifying significant fibrosis, with comparable AUROC values (0.68 and 0.67, respectively), supporting their limited discriminative performance. Importantly, the BARD score may be preferred in clinical practice due to its simplicity and the absence of indeterminate zones. In a large Asian MASLD cohort, the SAFE score demonstrated higher AUROC values than those observed in our study, in which fibrosis status was assessed histologically.[27] Differences between

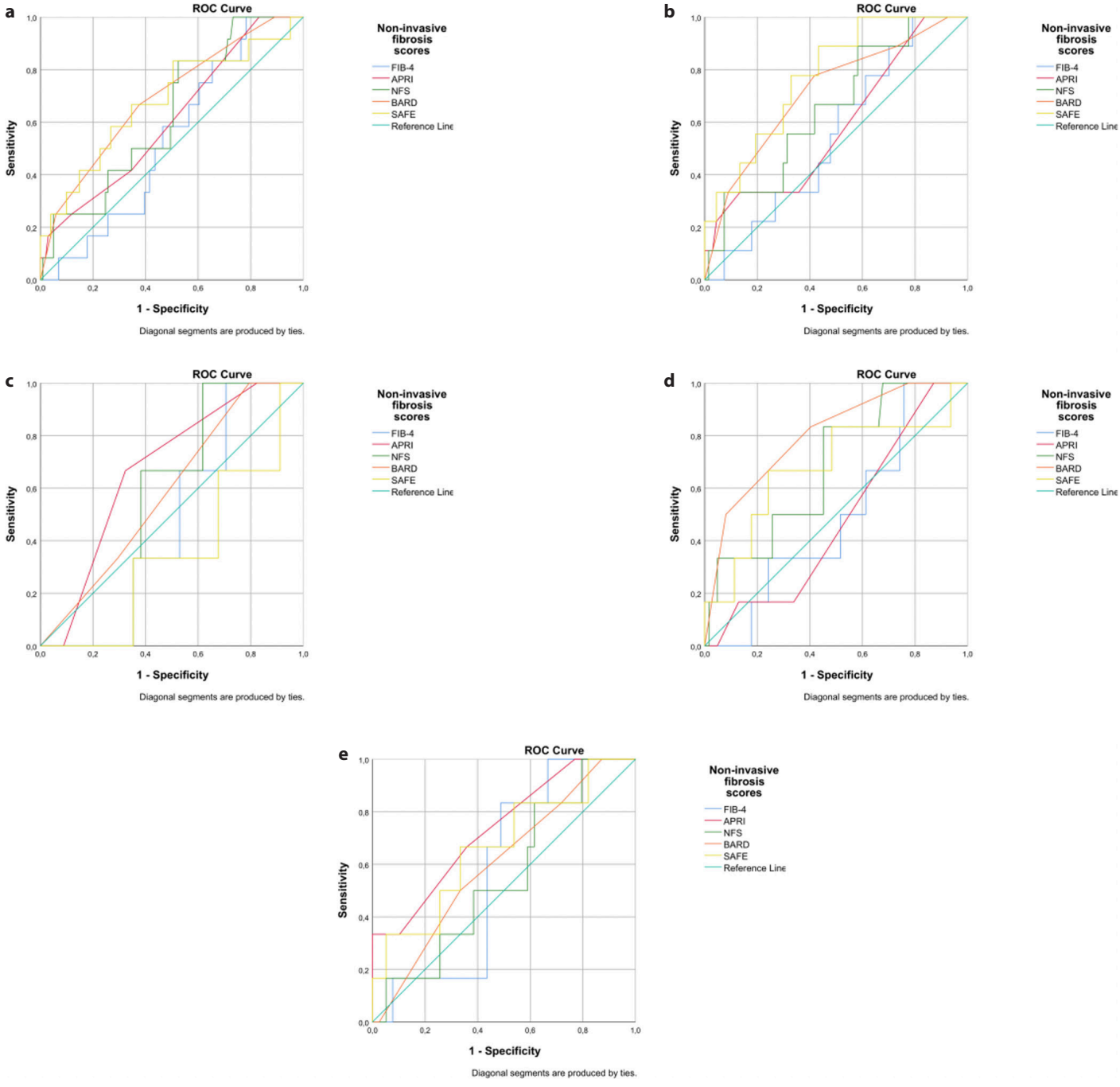


Figure 1. ROC curve analysis of serum-based fibrosis scores in detecting significant fibrosis in the whole cohort **(a)** and MASLD **(b)**, non-MASLD **(c)**, MTX user **(d)**, MTX non-user **(e)** subgroups.

APRI: Aspartate aminotransferase-to-platelet ratio index; BARD: Body mass index; aspartate aminotransferase–alanine aminotransferase ratio; and diabetes; FIB-4: Fibrosis-4 score; MASLD: Metabolic dysfunction-associated steatotic liver disease; MTX: Methotrexate; NFS: Non-alcoholic fatty liver disease fibrosis score; ROC: Receiver operating characteristic curve; SAFE: Steatosis-associated fibrosis estimator.

biopsy-based and VCTE-based reference standards likely explain this discrepancy. Despite lower AUROC values, all fibrosis scores in our study demonstrated high NPVs, supporting their clinical utility for ruling out significant fibrosis rather than confirming it. In contrast, PPVs were low, underscoring that elevated scores should prompt further evaluation rather than be considered diagnostic.

From a clinical perspective, our findings suggest that serum-based fibrosis scores may help identify patients less likely to have significant fibrosis and have a role in preliminary risk stratification among patients with psoriasis in dermatology clinics, particularly in settings with limited access to VCTE. Low SAFE or BARD scores in patients with MASLD, and low APRI scores in those without MASLD, can be considered for pre-

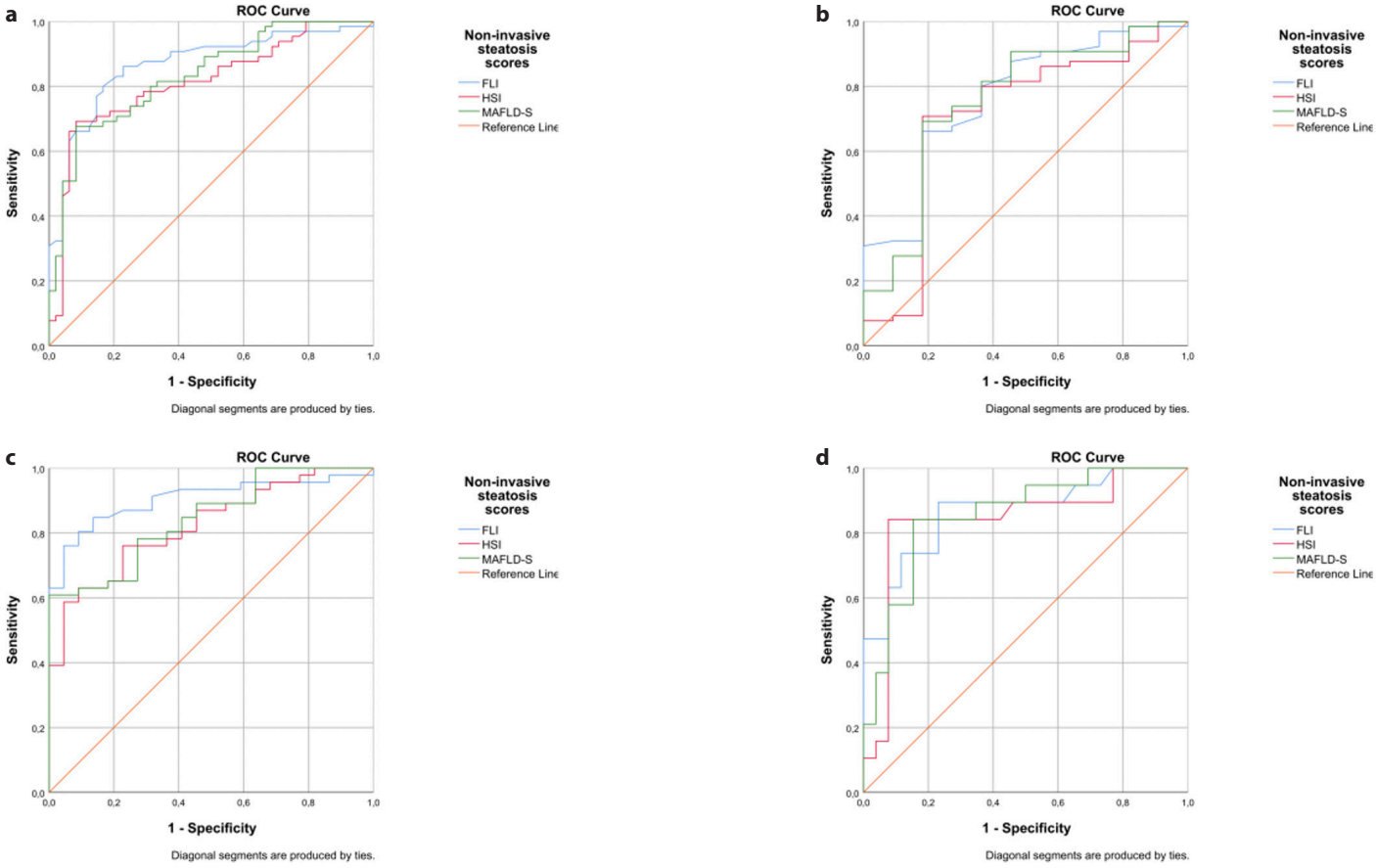


Figure 2. ROC curve analysis of serum-based steatosis scores in detecting significant steatosis in the whole cohort **(a)** and MASLD **(b)**, MTX user **(c)**, MTX non-user **(d)** subgroups.

FLI: Fatty liver index; HSI: Hepatic steatosis index; MAFLD-S: Metabolic dysfunction–associated fatty liver disease screening score; MASLD: Metabolic dysfunction–associated steatotic liver disease; MTX: Methotrexate; ROC: Receiver operating characteristic curve.

liminary triage in excluding significant fibrosis. However, these scores should not be used as standalone diagnostic tools, and abnormal/elevated results should be confirmed by elastography. The clinical utility of these non-invasive indices is further strengthened by the fact that the results obtained from established cut-off values parallel our exploratory findings, highlighting that while these tools have limited PPV, their high NPVs make them excellent preliminary triage instruments for ruling out significant fibrosis and steatosis in routine clinical practice. The steatosis scores evaluated in this study showed consistently strong performance. FLI, in particular, demonstrated excellent discriminative performance, although optimal cut-off values were higher than those reported in general populations, likely reflecting higher BMI and greater central obesity in patients with psoriasis. Data on the performance of MAFLD-S in patients with psoriasis are scarce, and our findings suggest that it may also serve as a practical screening tool in this population.

The diagnostic accuracy of serum-based NITs is known to vary significantly across different clinical settings. For instance, factors such as advanced age, type 2 diabetes, or obesity often lead to higher false-positive rates in scores like FIB-4 and NFS.[28,29] Paradoxically, despite the high prevalence of obesity (32.7%) and a high median BMI (28.7 kg/m^2) in our cohort, the study-derived exploratory cut-offs for fibrosis scores were notably lower than established values. This suggests that in patients with psoriasis, significant liver involvement may occur at lower biochemical thresholds, potentially masked by the systemic inflammatory nature of the disease. Furthermore, as highlighted in recent literature, clinicians should exercise caution when interpreting these scores in patients with varying transaminase levels, as elevated enzymes can disproportionately inflate biochemical-based indices and affect the accuracy of fibrosis assessment.[30] By considering these factors, our study underscores the importance of a personalized approach when using NITs for liver risk stratification in the psoriasis population.

In the present study, we focused on distinguishing patients with no or mild fibrosis from those with significant fibrosis (F2–F4), rather than advanced fibrosis alone. This approach is clinically relevant, as fibrosis stage F2 or higher is associated with disease progression and has direct implications for MTX discontinuation in the management of psoriasis. In addition, the limited number of patients with advanced fibrosis precluded meaningful analyses restricted to F3–F4 disease.

Several limitations should be acknowledged. First, this was a single-center study with a modest sample size, and only a small number of patients had significant fibrosis, limiting statistical precision and making subgroup analyses inherently exploratory. Notably, explor-

atory analyses for advanced fibrosis could not be performed due to the low number of events. Although NPV values were high, this should be interpreted in the context of the low prevalence of significant fibrosis in the cohort. Therefore, the observed NPV values do not necessarily indicate strong standalone test performance. Nevertheless, the prospective collection and evaluation of all clinical, biochemical, and elastographic data may have strengthened our findings compared to those obtained from retrospective studies, and low score values may still have practical triage utility as part of a stepwise assessment strategy. Second, liver biopsy was not performed in our study; therefore, this should not be interpreted as a histologically validated diagnostic study. Instead, the analyses reflect the concordance and discrimination of serum-based scores against VCTE-defined fibrosis and steatosis categories. Third, the cut-off values derived from this dataset are exploratory and should not be considered definitive or broadly generalizable without external validation. Finally, MASLD diagnosis was based on routinely available metabolic parameters, and some metabolic risk factors could not be assessed in all patients.

Conclusion

In patients with psoriasis, commonly used serum-based fibrosis scores demonstrated limited discriminative performance for detecting significant fibrosis; they represent valuable triage tools for ruling out significant fibrosis, particularly in resource-limited settings with restricted access to VCTE. In contrast, steatosis scores, particularly FLI, showed high reliability and good discrimination for detecting significant steatosis. To better elucidate their impact on clinical decision-making, large-scale, prospective, multicenter studies evaluating these scores in patients with psoriasis are warranted.

Online Appendix Link: https://file.paplino.com/hepatologyforum/files/1785246202-appendix-en.pdf

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