

# Diagnostic Performance of APRI, FIB-4, and NFS to Estimate Liver Fibrosis in Hepatic Sarcoidosis

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## BACKGROUND & AIMS

Most patients with sarcoidosis have some degree of hepatic involvement, which can lead to significant liver fibrosis and cirrhosis in some patients.

Non-invasive tests (NITs) could be used in sarcoidosis to:

1. Identify patients at low risk of fibrosis who could avoid unnecessary liver biopsies, and
2. Detect patients at high risk of fibrosis who should avoid methotrexate.

**Aim:** To assess the diagnostic performance of three simple NITs (APRI, FIB-4, and NAFLD Fibrosis Score) to estimate the degree of fibrosis in hepatic sarcoidosis when compared to liver biopsy.

## METHODS

- We included patients with biopsy-proven hepatic sarcoidosis within UNC Health diagnosed from 2014-2021.

- Subjects were categorized based on findings on biopsy using the METAVIR scoring system (F0-F4):

F0	No fibrosis
F1	Portal fibrosis without septa
F2	Portal fibrosis and few septa
F3	Numerous septa without cirrhosis
F4	Cirrhosis

- Labs collected closest to biopsy date within a +/-6-months were used to calculate three NITs:

NIT	Formula
APRI (AST to Platelet Ratio Index)	$(AST \text{ in IU/L}) / (AST \text{ Upper Limit of Normal in IU/L}) / (\text{Platelets in } 10^9/L)$
FIB-4 (Fibrosis-4 score)	$(Age * x \text{ AST}) / (\text{Platelets} * \sqrt{ALT})$
NFS (NAFLD Fibrosis Score)	$-1.675 + (0.037 * \text{age [years]}) + (0.094 * \text{BMI [kg/m}^2]) + (1.13 * \text{IFG/diabetes [yes = 1, no = 0]}) + (0.99 * \text{AST/ALT ratio}) - (0.013 * \text{platelet count [x}10^9/L]) - (0.66 * \text{albumin [g/dl]})$

- AUROC curves and logistic regression were used to determine optimal NIT thresholds and their predictive accuracy.
- Two thresholds were then selected for their ability to rule in advanced fibrosis (F3-F4) and rule out advanced fibrosis ( $\leq$ F2) with optimized accuracy.
- Performance of previously validated cut-offs was also examined.

## RESULTS

	Median	IQR	
Age	48 years	(40-54)	
	N	%	
Sex	Female	25	56.6%
	Male	20	44.4%
Race	Black	31	68.9%
	White	13	28.9%
	Unknown	1	2.2%
Labs	Median	IQR	
AST	60 U/L	(34-79)	
ALT	54 U/L	(34-81)	
Alk Phos	177 U/L	(97-431)	

Table 1: Patient Characteristics

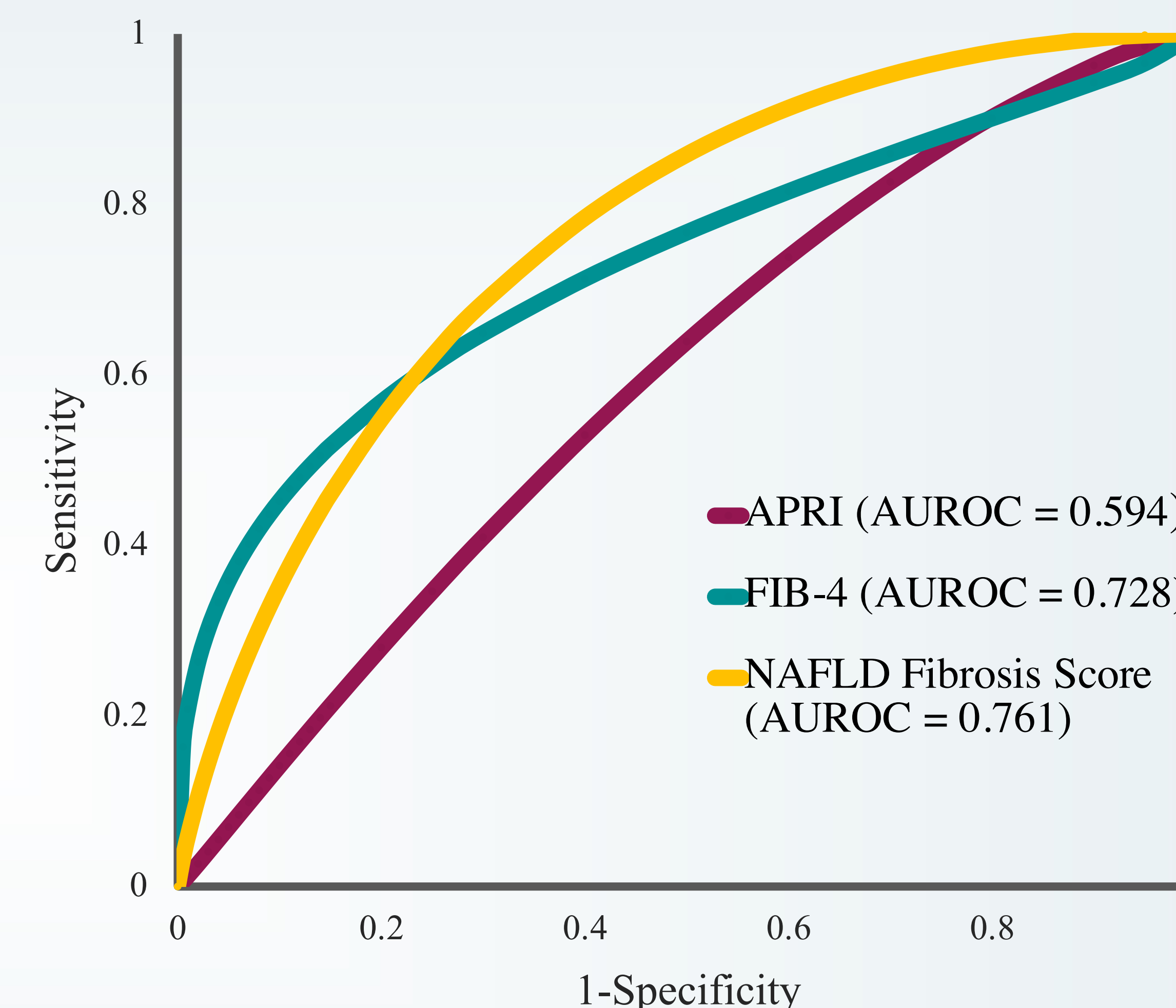


Figure 1: ROC Curves

NIT	Fibrosis Stage	Optimal Thresholds	Sensitivity	Specificity	Validated Thresholds	Sensitivity	Specificity
APRI	$\leq$ F2	$\leq$ 0.330	88%	19%	$\leq$ 1	38%	78%
	F3-F4	$\geq$ 1.179	25%	89%	$\geq$ 1.5	0%	92%
FIB-4	$\leq$ F2	$\leq$ 0.778	88%	19%	$\leq$ 1.3	75%	54%
	F3-F4	$\geq$ 2.361	38%	89%	$\geq$ 2.67	38%	92%
NAFLD Fibrosis Score	$\leq$ F2	$\leq$ -2.322	88%	35%	$\leq$ -1.455	75%	43%
	F3-F4	$\geq$ 0.928	32%	90%	$\geq$ 0.676	50%	92%

Table 2: Thresholds and Test Characteristics for NITs for Determining Advanced Fibrosis

A high threshold (optimized for a specificity of  $\geq$ 85%) and low threshold (optimized for a sensitivity of  $\geq$ 85%) were selected to stratify patients as high versus low risk of advanced fibrosis with optimal accuracy.

## RESULTS

- The cohort consisted of 45 subjects, including 8 (18%) with advanced fibrosis (F3 or F4) on liver biopsy.
- Subjects had a median age of 48 years and were predominantly female overall was 56% female (55.6%) and Black (68.9%).
- The AUROCs for APRI, FIB-4, and NAFLD Fibrosis Score were 0.594, 0.728, 0.761.
- Sensitivity of all NITs for ruling out advanced fibrosis was 88% at optimal low thresholds, and specificity of all NITs for ruling in advanced fibrosis was 92% at validated high thresholds.

## CONCLUSION

- **FIB-4 and NAFLD Fibrosis Score were able to discriminate advanced fibrosis in patients with hepatic sarcoidosis with an acceptable level of accuracy.**
- External validation of these cut-offs for identifying fibrosis will be needed.

## REFERENCES

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