

Functional Liver Imaging Score on gadoxetic acid-enhanced MRI: correlation with MELD, ALBI, Child-Pugh, FIB-4, and diagnostic performance for advanced hepatic dysfunction in chronic liver disease

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ABSTRACT

Aims: The objective was to evaluate the diagnostic performance of the Functional Liver Imaging Score (FLIS) for the identification of severe hepatic dysfunction and the relationship between the FLIS on gadoxetic acid-enhanced MRI and established liver function scores in patients with chronic liver disease (CLD).

Methods: 104 patients with chronic liver disease who had gadoxetic acid-enhanced MRIs between January 2021 and December 2024 were the subjects of this retrospective study. Twenty-minute hepatobiliary phase images were used to score FLIS (0-6) based on portal vein signal intensity, biliary excretion, and parenchymal enhancement. The MELD, ALBI, Child-Pugh, and FIB-4 scores were computed using laboratory data obtained within two weeks before MRI.

Results: FLIS correlated with key biochemical markers of hepatic reserve (higher albumin and sodium; lower bilirubin and cholestatic/hepatocellular enzymes; all $p < 0.001$) and showed strong correlations with MELD and ALBI ($r = -0.63$ each). Mean FLIS decreased from Child-Pugh A (5.66 ± 0.53) to B (3.85 ± 1.32) to C (1.57 ± 0.79) ($p < 0.001$). FLIS demonstrated high diagnostic accuracy for advanced dysfunction, with AUCs of 0.86 for MELD > 5 and 0.94 for Child-Pugh B/C.

Conclusion: FLIS has high correlations with biochemical and composite scores of liver function and can well predict severe hepatic dysfunction. The moderate correlation of FLIS with FIB-4 indicates that FLIS is more a measure of functional reserve than fibrosis and thus confirms its utility as an imaging biomarker.

Keywords: Functional Liver Imaging Score, chronic liver disease, MELD, ALBI, Child-Pugh, FIB-4

INTRODUCTION

Chronic liver disorders represent a major global health burden, with prevalence estimates reaching hundreds of millions internationally.^{1,2} To predict prognosis, guide treatment choices, and evaluate surgical or interventional risks in these patients, an accurate evaluation of hepatic functional reserve is crucial.³

Traditionally, liver function has been measured using laboratory-based tools such as the Child-Pugh, albumin-bilirubin (ALBI) scores and Model for End-Stage Liver Disease (MELD).⁴⁻⁶

Although carefully validated, these indices are influenced by acute biochemical fluctuation, systemic illness, and renal

function and are not regionally specific with respect to hepatic function.^{7,8} Consequently, interest in non-invasive, image-based biomarkers that directly reflect hepatocellular function is growing.

Magnetic resonance imaging (MRI) performed with gadoxetic acid allows evaluation of both liver morphology and contrast-related functional characteristics in the same examination.⁹ The uptake of gadoxetic acid depends mainly on organic anion transporting polypeptides (OATP)-mediated transport into hepatocytes, whereas its biliary elimination requires multidrug resistance-associated protein 2 (MRP2)-related excretion pathways.^{10,11}



The Functional Liver Imaging Score (FLIS), first described by Bastati et al.,¹² is a simple semi-quantitative scoring system that uses three variables from hepatobiliary phase MRI: parenchymal enhancement, biliary excretion, and portal vein signal intensity.

Several studies have demonstrated associations between FLIS and biochemical liver function tests, clinical scores, and postoperative outcomes.¹²⁻¹⁸ However, data directly comparing FLIS with a comprehensive panel of widely used liver function and fibrosis indices, including MELD, ALBI, Child-Pugh, and FIB-4, in a single mixed-etiology chronic liver disease (CLD) cohort remain limited.

Therefore, the primary aim of this study was to assess the correlation between FLIS and established liver function scores (MELD and ALBI) in patients with CLD. Secondary aims were to evaluate its relationship with Child-Pugh class and FIB-4, and to determine the diagnostic performance of FLIS for identifying advanced hepatic dysfunction.

METHODS

Ethics

The study was carried out with the permission of the Ankara Bilkent City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 19.11.2025, Decision No: TABED 1-25-1842). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Population

All consecutive patients who underwent gadoteric acid-enhanced liver MRI between January 2021 and December 2024 were screened for eligibility. CLD was a mandatory inclusion criterion and was confirmed by at least one of the following: (1) a documented diagnosis of chronic hepatitis, fibrosis, or cirrhosis by a hepatologist or gastroenterologist; (2) characteristic imaging findings of CLD or cirrhosis, including nodular liver contour, segmental volume redistribution, caudate lobe hypertrophy, splenomegaly, or portosystemic collaterals; and/or (3) a documented chronic etiology (e.g., hepatitis B or C infection >6 months, alcohol-related liver disease, or metabolic-associated steatotic liver disease) with supportive clinical and laboratory findings. Etiology of CLD was determined from clinical records and categorized as viral, alcohol-related, or metabolic/cryptogenic.

Eligibility criteria included availability of hepatobiliary-phase images acquired ≥ 20 minutes after contrast administration, laboratory and clinical data obtained within two weeks of MRI, and absence of focal hepatic lesions involving more than one liver segment. During the study period, 312

consecutive gadoteric acid-enhanced MRI examinations were screened. Patients were excluded due to absence of a 20-minute hepatobiliary phase (n=15), laboratory or clinical data obtained more than two weeks from MRI (n=24), severe motion or breathing artefacts (n=51), portal vein thrombosis (n=11), prior hepatic surgery (n=32), or focal hepatic lesions involving more than one Couinaud segment (n=75). After applying these predefined exclusion criteria, 104 patients with CLD were included in the final analysis.

MRI Acquisition

All MR examinations were performed on a 3.0-T scanner (SIGNA, GE HealthCare, Waukesha, WI, USA) using a phased-array abdominal coil. Patients were imaged in the supine position. The protocol consisted of axial and coronal T2-weighted sequences (typical field of view 38-40 cm, TR/TE approximately 3750-4280/90 ms, slice thickness 5 mm, matrix 320-352×224-230) and T1-weighted sequences (FOV 40-44 cm, TR/TE 4.2-4.9/2.3-2.6 ms, slice thickness 4 mm, matrix 260-300×162-200).

Gadoxetic acid (Gd-EOB-DTPA, Primovist®, Bayer Healthcare) was delivered intravenously at a dosage of 0.025 mmol/kg, succeeded by a 30-ml saline flush. Hepatobiliary phase images were acquired 20 minutes after injection.

FLIS Assessment

FLIS was assessed on hepatobiliary phase images according to the criteria described by Bastati et al.¹² FLIS was derived by visually evaluating hepatobiliary-phase images in terms of (1) the relative brightness of the liver compared with the kidney, (2) the clarity of intrahepatic biliary ducts, and (3) the appearance of the portal vein compared with parenchyma. Each component contributes 0-2 points to the composite score, and the total FLIS was obtained by summation (range, 0-6) (Table 1, Figure 1).

An abdominal radiologist with 10 years of experience, blinded to laboratory values and clinical data, scored all examinations independently.

Laboratory and Clinical Data

All laboratory tests were performed within two weeks of the MRI examination. The following parameters were recorded: serum bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), international normalized ratio (INR), creatinine, serum sodium, and platelet count. Clinical liver function scores were calculated as follows: Child-Pugh score and class (A-C), MELD score, ALBI score and grade ($ALBI = [\log_{10} \text{bilirubin} \times 0.66] + [\text{albumin} \times 0.085]$), and FIB-4 index ($FIB-4 = [\text{age} \times \text{AST}] / [\text{platelet count} \times \sqrt{\text{ALT}}]$). All scores were calculated using the laboratory values closest to the MRI date.

Table 1. Functional Liver Imaging Score (FLIS) parameters evaluated on hepatobiliary-phase magnetic resonance imaging (MRI)

Parameter	Score 0	Score 1	Score 2
Parenchymal enhancement (compared with renal cortex)	Lower than renal cortex	Equal to renal cortex	Higher than renal cortex
Biliary excretion	No visible intrahepatic bile ducts	Faint visualization of bile ducts	Distinct visualization of intrahepatic bile ducts
Portal vein signal intensity (relative to liver parenchyma)	Hyperintense	Isointense	Hypointense



Figure 1. Gadoteric acid-enhanced hepatobiliary phase MRI in a 55-year old man with advanced chronic liver disease.

The Functional Liver Imaging Score is 1, based on absent intrahepatic biliary excretion (score 0), liver parenchymal signal intensity equal to the renal cortex (score 1), and hyperintense portal vein relative to the liver parenchyma (score 0). These imaging findings are concordant with severe hepatic dysfunction, as reflected by a MELD score of 18, Child-Pugh class C, and ALBI grade 3

MRI: Magnetic resonance imaging, MELD: Model for End-Stage Liver Disease, ALBI: Albumin-bilirubin

Statistical Analysis

All statistical computations were carried out using SPSS (version 26; IBM), and analyses were tailored to the distributional properties of each variable.

Quantitative measures are summarized as means \pm SD or medians and interquartile ranges, whichever was appropriate, given the distribution. Categorical data are described as absolute numbers and proportions. Distributional characteristics of numeric variables were assessed using the Shapiro-Wilk procedure. Between-group differences were investigated by parametric or non-parametric tests according to the distribution of the data: ANOVA or the Kruskal-Wallis test.

The main analysis examined the association of FLIS with MELD and ALBI scores using Spearman's rank correlation coefficient (r) with associated 95% confidence intervals (CIs). Secondary analyses explored associations between FLIS and other biochemical measures and FIB-4.

ROC analysis was performed to assess the diagnostic performance of FLIS for detecting advanced liver dysfunction defined as MELD >15 , Child-Pugh class B/C versus class A, and FIB-4 ≥ 3.25 . AUCs and 95% CIs were calculated for all endpoints investigated. Thresholds reflecting the best balance between sensitivity and specificity were selected based on Youden's method. A two-sided p -value <0.05 was considered statistically significant.

Additional analyses were conducted to assess whether the FLIS provided independent and incremental value beyond the established biochemical indices.

To assess incremental discrimination, the AUC was calculated for both the base model and the extended model.

RESULTS

The study included 104 participants with chronic liver disease. Fifty-two percent were male, and the average age was 54.1 \pm 11.1 years. **Table 2** summarizes the clinical, laboratory, and demographic features of each patient in the study. The cohort included a mixed etiologic spectrum, reflecting real-world clinical practice.

FLIS scores correlated significantly with both the biochemical and composite parameters of liver function.

Table 2. Baseline demographic, clinical and laboratory characteristics of the study population (n=104)

Parameter	Value
Age (years)	54.1 \pm 11.1
Male sex, n (%)	54 (52)
Etiology of chronic liver disease, n (%)	
Hepatitis B	49 (47)
Hepatitis C	21 (20)
Alcohol-related	11 (11)
NASH/cryptogenic	23 (22)
Child-Pugh score	7 \pm 2
Class A/B/C, n (%)	71 (68.3%)/26 (25.0%)/7 (6.7%)
MELD score	13 \pm 5
ALBI score	-1.8 \pm 0.6
Grade 1/2/3, n (%)	38 (36.5%)/47 (45.2%)/19 (18.3%)
FIB-4 index	4.8 \pm 2.9
Serum albumin (g/dl)	3.4 \pm 0.6
Total bilirubin (mg/dl)	1.9 \pm 1.7
INR	1.3 \pm 0.3
AST (U/L)	65 \pm 38
ALT (U/L)	52 \pm 44
ALP (U/L)	138 \pm 58
Platelet count ($\times 10^3/\mu\text{L}$)	122 \pm 61
Serum sodium (mmol/L)	138 \pm 4
Creatinine (mg/dl)	0.9 \pm 0.3
FLIS score	4.9 \pm 1.6
FLIS by Child-Pugh class (A/B/C)	5.7 \pm 0.5/3.8 \pm 1.3/1.6 \pm 0.8
Values are presented as mean \pm SD or n (%). AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase	

FLIS correlated positively with albumin ($r=0.56$, $p<0.001$) and serum sodium ($r=0.40$, $p<0.001$), and negatively with bilirubin ($r=-0.59$, $p<0.001$), AST ($r=-0.53$, $p<0.001$), ALP ($r=-0.51$, $p<0.001$), and INR ($r=-0.32$, $p<0.001$). Among composite indices, FLIS showed strong negative correlations with ALBI score ($r=-0.63$, $p<0.001$) and MELD score ($r=-0.63$, $p<0.001$), and a moderate negative correlation with FIB-4 ($r=-0.33$, $p<0.001$).

When categorized according to the Child-Pugh classification, FLIS decreased sequentially from Class A (5.66 \pm 0.53) to Class B (3.85 \pm 1.32) to Class C (1.57 \pm 0.79) ($p<0.001$, Kruskal-Wallis test) (**Figure 2**).

When the MELD score was categorized as ≤ 10 , 11-18 and >18 , the respective mean FLIS values were 5.8 \pm 1.1, 4.3 \pm 1.4 and 2.2 \pm 1.1 ($p<0.001$) (**Figure 2**).

Post hoc analysis also confirmed that FLIS decreased significantly in both the 11-18 and >18 groups compared with the ≤ 10 group (Bonferroni-corrected $p<0.01$).

Similarly, FLIS decreased stepwise along ALBI grades: Grade 1 (5.7 \pm 1.0), grade 2 (4.1 \pm 1.3) and grade 3 (2.4 \pm 1.0) ($p<0.001$) (**Figure 2**).

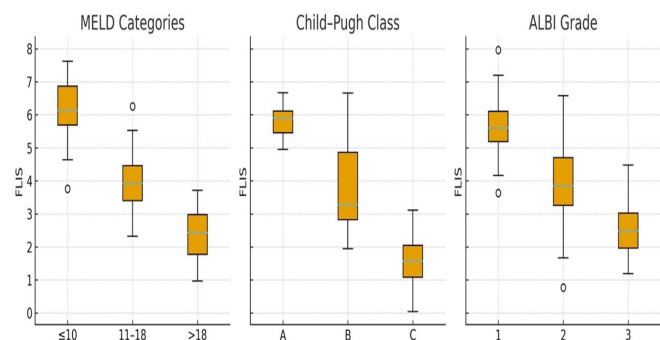


Figure 2. Boxplots showing the distribution of FLIS according to (A) MELD categories, (B) Child-Pugh class, and (C) ALBI grade
FLIS: Functional Liver Imaging Score, MELD: Model for End-Stage Liver Disease, ALBI: Albumin-bilirubin

Thirty-three patients (32%) were classified as Child-Pugh class B/C. In a multivariable logistic regression model including age, sex, and ALBI grade, higher ALBI grade was independently associated with Child-Pugh class B/C (OR per 1-grade increase, 6.9; 95% CI, 1.8-18.2; $p=0.034$). When FLIS was added to this model, it remained a strong and independent predictor of advanced clinical stage.

The discriminative ability of the base model (age, sex, ALBI grade) for identifying Child-Pugh class B/C was high, with an AUC of 0.88 (95% CI, 0.81-0.95). Addition of FLIS further improved classification, increasing the AUC to 0.96 (95% CI, 0.92-0.99) (Figure 3). The incremental gain in AUC was 0.07 (95% CI, 0.03-0.13) based on bootstrap resampling, indicating significant added prognostic value of FLIS beyond biochemical indices alone.

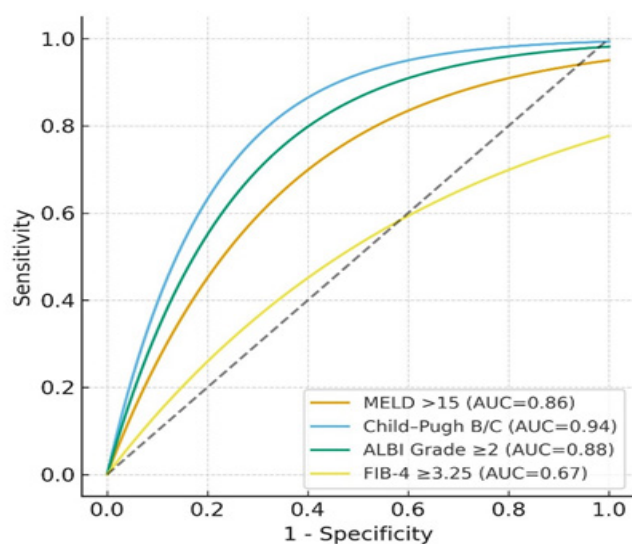


Figure 3. Receiver operating characteristic (ROC) curves demonstrating the diagnostic performance of the Functional Liver Imaging Score (FLIS) for identifying advanced hepatic dysfunction

Using the optimal FLIS threshold of ≤ 5 , the sensitivity for predicting MELD >15 was 100% (95% CI, 75-100%), and the negative predictive value was 100% (95% CI, 93-100%), while specificity was 55% and the positive predictive value was 24% (Table 3).

DISCUSSION

In this single-center cohort of patients with chronic liver disease, we found that FLIS derived from gadoteric

Metric	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
FLIS ≤ 5	1.00 (0.75-1.00)	0.55 (0.44-0.65)	0.24	1.00
ALBI grade ≥ 2	0.85 (0.55-0.98)	0.51 (0.40-0.61)	0.20	0.96
Child-Pugh B/C	1.00 (0.75-1.00)	0.78 (0.68-0.86)	0.39	1.00

CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value, FLIS: Functional Liver Imaging Score, MELD: Model for End-Stage Liver Disease, ALBI: Albumin-bilirubin

acid-enhanced MRI correlated strongly with established biochemical and clinical measures of liver function, including MELD, ALBI, and Child-Pugh scores, while showing only moderate association with the fibrosis-based FIB-4 index. These findings support the concept that FLIS primarily reflects hepatocellular functional reserve and transporter activity, rather than structural fibrosis alone.

Our multivariable modeling shows that FLIS provides information that is independent from established biochemical markers of liver function. Specifically, after adjustment for age, sex, and ALBI grade, every 1-point decrease in FLIS increased the odds of being Child-Pugh class B/C by approximately 11-fold. Notably, the addition of FLIS to a model that contained ALBI grade increased the AUC for identifying Child-Pugh B/C from 0.88 to 0.96, reflecting a statistically and clinically meaningful improvement in discriminative capability. Such findings support the contention that FLIS reflects aspects of hepatocellular functional reserve that are not fully captured by laboratory-based scores in isolation. Moreover, the weaker relationship between FLIS and FIB-4 underscores its functional rather than structural biomarker status. Collectively, these results position FLIS as a complementary imaging tool that enhances risk stratification when combined with established biochemical indices. Our results complement and extend previous studies that have linked FLIS to Child-Pugh class, ALBI grade, and postoperative outcomes by providing a comprehensive comparison with MELD, ALBI, Child-Pugh, and FIB-4 in a mixed-etiology CLD population and by demonstrating high diagnostic performance of FLIS for advanced hepatic dysfunction. The mechanisms behind FLIS's diagnostic validity are biologically plausible.¹²⁻¹⁸

Gadoxetic acid uptake is governed by hepatocellular transport mechanisms involving OATP family carriers, while its excretion into bile depends on canalicular efflux pathways such as MRP2,8,10. The transport processes may be impaired due to hepatocellular dysfunction or cholestasis, resulting in diminished hepatobiliary-phase signal intensity and reduced FLIS scores. Thus, FLIS provides a direct measure of hepatocellular transporter function, which is a vital aspect of hepatic reserve that cannot be determined by structural fibrosis alone.

In line with this physiology, our study found strong inverse correlations between FLIS and bilirubin ($r=-0.59$), INR ($r=-0.32$), AST ($r=-0.53$) and ALP ($r=-0.51$) and positive correlations with albumin ($r=0.56$) and serum sodium ($r=0.40$). These biochemical correlations confirm that FLIS reflects both hepatocellular synthetic capacity and transporter-mediated excretory function.

The Child-Pugh score is still one of the most widely used for staging cirrhosis and predicting prognosis. However, it incorporates subjective criteria such as ascites and encephalopathy, which are susceptible to clinical heterogeneity and treatment variation, and which can lead to misclassification of functional status.^{19,20} Unlike the Child-Pugh system, ALBI relies exclusively on bilirubin and albumin values and avoids subjective clinical variables.^{4,21}

Various studies have demonstrated that the ALBI score is more effective than the Child-Pugh score at predicting prognosis, particularly in cases of hepatocellular carcinoma and in surgical populations.²²⁻²⁶

In our study population, FLIS decreased stepwise in both Child-Pugh classes and ALBI grades, reflecting the expected deterioration in liver function. This simultaneous behavior indicates that FLIS, ALBI and Child-Pugh all describe the same biological range of hepatocellular function, but in different ways. Child-Pugh scores the clinical aspects, ALBI scores the objective laboratory values, and FLIS scores the essential imaging findings of hepatobiliary transport capability. These scores are complementary, and this enhances the utility of FLIS as a non-invasive imaging surrogate for hepatic functional reserve that can be combined with existing scoring systems. FLIS scores were found to be monotonically decreasing with increasing MELD scores (≤ 10 , 11-18, and >18), suggesting a progressive reduction in hepatocellular functional reserve with worsening disease severity. The monotonic relationship suggests a strong correlation between imaging and biochemical parameters of liver dysfunction. Since MELD scores include bilirubin, INR, and creatinine, which can be affected by systemic factors, FLIS may reflect a more direct assessment of hepatocellular capability. A similar study by Sakai et al.¹⁴ found that FLIS is a better predictor of hepatectomy outcomes than MELD or ALBI scores in patients with normal liver function.

Our ROC analysis also confirmed that FLIS is highly discriminatory for severe hepatic dysfunction, with AUCs of 0.86 for MELD >5 and 0.94 for Child-Pugh B/C. These values are within the range reported for quantitative MR techniques such as T1 mapping and perfusion analysis in the literature, suggesting that a simple visual score like FLIS may offer comparable clinical utility with minimal additional post-processing.^{11,17}

The FIB-4 index, which was originally developed to evaluate the risk of advanced fibrosis in individuals with hepatitis C, is based on age, AST, ALT, and platelet count.^{27,28} It is also commonly used as an inexpensive, non-invasive method for ruling out or diagnosing significant fibrosis, according to threshold values of approximately 1.45 and 3.25. However, the FIB-4 index primarily reflects structural fibrotic burden rather than hepatocellular function. Therefore, we identified a moderate correlation between FLIS and FIB-4 (AUC=0.67 for FIB-4 ≥ 3.25), which is understandable on biological grounds given their differing pathophysiological foundations. The most recent large cohort population evidence appears to support the use of FIB-4 for predicting long-term liver-related events and mortality in clinical practice. However, it seems that for short-term functional markers such as portal hypertension and early outcomes, non-invasive fibrosis

scores such as FIB-4 are only associated to a limited extent, while ALBI is strongly associated with these functional outcomes.²⁹⁻³³ FLIS evaluates functional impairment, whereas FIB-4 reflects fibrotic burden two related but distinct processes in chronic liver disease.

Given its simplicity and reproducibility, FLIS may serve as an adjunct imaging biomarker that complements biochemical indices in clinical and surgical decision-making. Several recent studies have suggested that FLIS thresholds around $\leq 5-6$ may indicate clinically relevant impairment and postoperative risk.^{14,15,18} Our results confirm this range, confirming FLIS as a clinically effective measure in surgery and treatment planning.

Limitations

First, its retrospective, single-center design may introduce selection bias, and the relatively small number of patients with advanced disease (Child-Pugh C or very high MELD scores) limits the precision of estimates in these subgroups. Second, laboratory tests were allowed within a two-week window of MRI, during which liver function may fluctuate, particularly in decompensated patients. Third, FLIS assessment was performed by a single reader and interobserver variability was not assessed; although prior studies suggest good reproducibility, this should be confirmed in future multicenter work. Fourth, FIB-4 thresholds were originally derived in hepatitis C populations and were applied here to a mixed-etiology CLD cohort, which may partly explain the only moderate association between FLIS and FIB-4. Finally, we did not evaluate hard clinical outcomes such as decompensation, liver-related mortality, or post-hepatectomy liver failure, and future prospective studies are warranted to establish the prognostic value of FLIS in these settings.

CONCLUSION

FLIS values derived from gadoteric acid-enhanced MRI show strong correlations with MELD, ALBI, and Child-Pugh scores and accurately distinguish advanced hepatic dysfunction in patients with chronic liver disease. The only moderate association with FIB-4 suggests that FLIS predominantly reflects functional rather than structural impairment. In addition to strong univariable correlations, FLIS demonstrated independent and incremental prognostic value beyond ALBI for identifying advanced hepatic dysfunction, supporting its use as a practical imaging biomarker to complement existing liver function scores in risk stratification and treatment planning.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Bilkent City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 19.11.2025, Decision No: TABED 1-25-1842).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The author declare no conflicts of interest related to this study.

Financial Disclosure

The author received no financial support for the conduct or publication of this research.

Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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