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Original Article

Performance of Noninvasive Indices for Discrimination of Metabolic Dysfunction-Associated Steatotic Liver Disease in Young Adults

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Background/Aims: Although numerous noninvasive steatosis indices have been developed to assess hepatic steatosis, whether they can be applied to young adults in the evaluation of metabolic dysfunction-associated steatotic liver disease (MASLD) remains uncertain.

Methods: Data from patients under 35 years of age who visited the Liver Health Clinic at the Armed Forces Goyang Hospital between July 2022 and January 2024 were retrospectively collected. Steatosis was diagnosed on the basis of a controlled attenuation parameter score ≥250 dB/m. MASLD was defined as the presence of steatosis in patients with at least one cardiometabolic risk factor.

Results: Among the 1,382 study participants, 901 were diagnosed with MASLD. All eight indices for diagnosing steatosis differed significantly between the MASLD and non-MASLD groups ($p<0.001$). Regarding the predictive performance, the hepatic steatosis index (HSI), fatty liver index (FLI), Framingham steatosis index, Dallas steatosis index, Zhejiang University index, lipid accumulation product, visceral adiposity index, and triglyceride glucose-body mass index exhibited an area under the curve of 0.898, 0.907, 0.899, 0.893, 0.915, 0.869, 0.791, and 0.898, respectively. The cutoff values for the FLI and HSI were re-examined, indicating a need for alternative cutoff values for the HSI, with a rule-in value of 42 and a rule-out value of 36 in this population.

Conclusions: This study presents novel findings regarding the predictive performance of established steatosis markers in young adults. Alternative cutoff values for the HSI in this population have been proposed and warrant further validation. **(Gut Liver 2025;19:116-125)**

Key Words: Biomarkers; Fatty liver; Metabolic dysfunction-associated steatotic liver disease; Young adult; Hepatic steatosis index

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) poses a significant socioeconomic burden, affecting approximately 30% of the global population.[1] The prevalence of NAFLD in Korea aligns closely with global statistics, reported to be 30% to 40% according to recent publications.[2,3] Notably, NAFLD is also prevalent among young adults, with an estimated prevalence of approximately 16%.[4] Recently, the term "metabolic dysfunction-associated steatotic liver disease (MASLD)" has emerged as a proposed replacement for NAFLD, underscoring the disease's association with cardiometabolic risk factors.[5] Given the substantial overlap between MASLD and NAFLD, encompassing approximately 97% to 98% of NAFLD cases, the epidemiological and noninvasive diagnostic approaches developed for NAFLD may seamlessly transition to MASLD without necessitating significant modifications.[6,7]

The assessment of MASLD requires confirmation of the presence of steatosis. Various tools are available for determining hepatic steatosis.[8] While liver biopsy is the gold standard for defining hepatic steatosis, its invasiveness limits its clinical utility.[9] Abdominal ultrasound represents another option widely used for identifying hepatic steatosis. However, given the increasing prevalence of MASLD, identifying noninvasive diagnostic tests for hepatic steatosis that are accessible and easy to use has become imperative.[10]

In this context, several noninvasive steatosis indices have been developed to diagnose NAFLD.[8] These indices have demonstrated acceptable performance in predicting NAFLD across various validation studies.[11,12] However, sufficient validation in the context of MASLD has not yet been achieved. Additionally, the derivation sets of these indices primarily consist of middle-aged to older populations, typically in their 40s or older, thereby limiting their applicability in younger cohorts. Furthermore, considering the suboptimal performance of noninvasive fibrosis indices in populations aged ≤35 years, the need for the validation of steatosis indices is unmet, specifically in younger populations.[13,14]

Although numerous studies have validated the predictive capabilities of various steatosis indices for NAFLD, studies investigating their performance in predicting MASLD are lacking.[8] Moreover, despite potential demographic differences between young MASLD patients and middle-aged to older MASLD patients, no study has validated steatosis indices in younger populations.[15] In light of these gaps, we aimed to validate and compare various steatosis indices for detecting MASLD in the young age group. In addition, we sought to assess the suitability of existing thresholds for the most used steatosis indices, such as the fatty liver index (FLI) and hepatic steatosis index (HSI) and propose alternative thresholds if necessary.

MATERIALS AND METHODS

1. Patients

We conducted a retrospective study using data selected consecutively from patients who visited the "Liver Health Clinic" at Armed Forces Goyang Hospital between July 2022 and January 2024. We included patients aged 18 to 35 years who underwent abdominal ultrasonography and vibration-controlled transient elastography. Patients were excluded if they met any of the following criteria: (1) evidence of viral hepatitis, including hepatitis A, B, or C; (2) acute hepatitis; or (3) a history of excessive alcohol consumption (>210 g/wk for men and >140 g/wk for women). This study was approved by the Institutional Review Board of the Korean Armed Forces Medical Command (IRB number: AFMC 2024-03-005) and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

2. Assessment of steatosis

The presence of steatosis was primarily evaluated using the controlled attenuation parameter (CAP) score measured using vibration-controlled transient elastography. Patients were instructed to fast for a minimum of 8 hours before the examination. The M probe was used in subject with a body mass index (BMI) under 30 kg/m^2 and the XL probe was used for those with a BMI over 30 kg/m^2.[16,17] CAP score of ≥250 dB/m was considered indicative of steatosis, following the reference values proposed by a prospective study conducted in Korea.[18] The degree of steatosis was further assessed using the reference scale proposed by the same study, categorized as follows: S1=250–299 dB/m, S2=299 dB/m–327 dB/m, and S3≥327 dB/m. The presence of steatosis, as determined by ultrasound, was also noted for sensitivity analysis.

3. Definition of MASLD

MASLD was diagnosed in patients exhibiting steatosis if they presented with one or more of the following cardiometabolic risk factors:[19] (1) BMI ≥23 kg/m^2 or waist circumference ≥90 cm for males and ≥85 cm for females;[20] (2) fasting serum glucose ≥100 mg/dL or hemoglobin A1c ≥5.7% or diagnosis of type 2 diabetes or treatment for type 2 diabetes; (3) blood pressure ≥130/85 mm Hg or the use of antihypertensive medication; (4) triglycerides ≥150 mg/dL or the use of lipid-lowering medications; and (5) high-density lipoprotein cholesterol ≤40 mg/dL for males and ≤50 mg/dL for females or the use of lipid-lowering medications.

4. Indices included for the analysis

Eight indices predictive of steatosis were included for analysis, comprising the following: HSI, FLI, Framingham steatosis index (FSI), Dallas steatosis index (DSI), Zhejiang University index (ZJU), lipid accumulation product (LAP), visceral adiposity index (VAI), and the triglyceride glucose-BMI (TyG-BMI).[21-28] The eight indices were calculated according to the formulae specified in the original articles (Supplementary Table 1).

5. Determining the cutoff values

Cutoff values for the steatosis indices were re-evaluated using the criterion proposed by Power *et al.*,[29] which sug-

gests that the sum of sensitivity and specificity should be at least 150% to qualify as a useful test. Therefore, rule-in and rule-out cutoff values for diagnosing MASLD were established to achieve specificity or sensitivity levels of approximately 90% while ensuring that the sum of sensitivity and specificity exceeded 150%.

6. Statistical analysis

The Student t-test was employed for continuous variables, and the results are presented as mean values with standard deviations. Categorical variables were analyzed using the chi-square or Fisher exact test, depending on the sample size. Linear regression analysis was conducted to identify the relationship between steatosis indices, and Pearson correlation coefficients were calculated to demonstrate the correlations between these indices. A correlation between two biomarkers was deemed strong if the correlation coefficient (r) exceeded 0.6 and moderate if the value fell between 0.4 and 0.6. Receiver operating characteristic curves were used to visually depict the diagnostic performance of each index. DeLong's test was used to compare the area under the receiver operating characteristic curves (AUROCs) of the included indices. An AUROC of 0.7 to 0.8 was considered fair accuracy, 0.8 to 0.9 as good accuracy, and values above 0.9 as excellent accuracy. Statistical significance was set at $p<0.05$. All statistical analyses were performed using the R statistical software (version 4.0.3; R Foundation Inc., Vienna, Austria; http://cran.r-project.org, accessed on April 3, 2024).

RESULTS

1. Baseline characteristics

After excluding patients who met the exclusion criteria, 1,382 individuals were included in the analysis (Fig. 1). Table 1 presents the baseline characteristics of the study population. The enrolled individuals were compared based on the presence of MASLD as determined by the CAP score. Overall, CAP scores were measured using the M probe for 1,046 individuals and the XL probe for 336 individuals. Males predominated the entire study cohort, comprising 98% of the total study population, with a mean age of 23.3 years. The mean values of BMI and waist circumference values were 27.8 kg/m² and 94.2 cm, respectively. Among the study population, 4.9% were diagnosed with diabetes mellitus, whereas 15.0% and 34.3% had hypertension and dyslipidemia, respectively.

Comparison between the MASLD (n=901) and non-MASLD groups (n=481) revealed that MASLD patients were older (23.5 years vs 22.9 years, p=0.024) and had higher BMI (29.8 kg/m² vs 24.1 kg/m², p<0.001) and waist circumference (100.0 cm vs 83.4 cm, p<0.001) than the non-MASLD group. The MASLD group had a higher proportion of patients with diabetes mellitus (6.2% vs 2.3%, p=0.002), hypertension (16.9% vs 11.4%, p=0.009), and

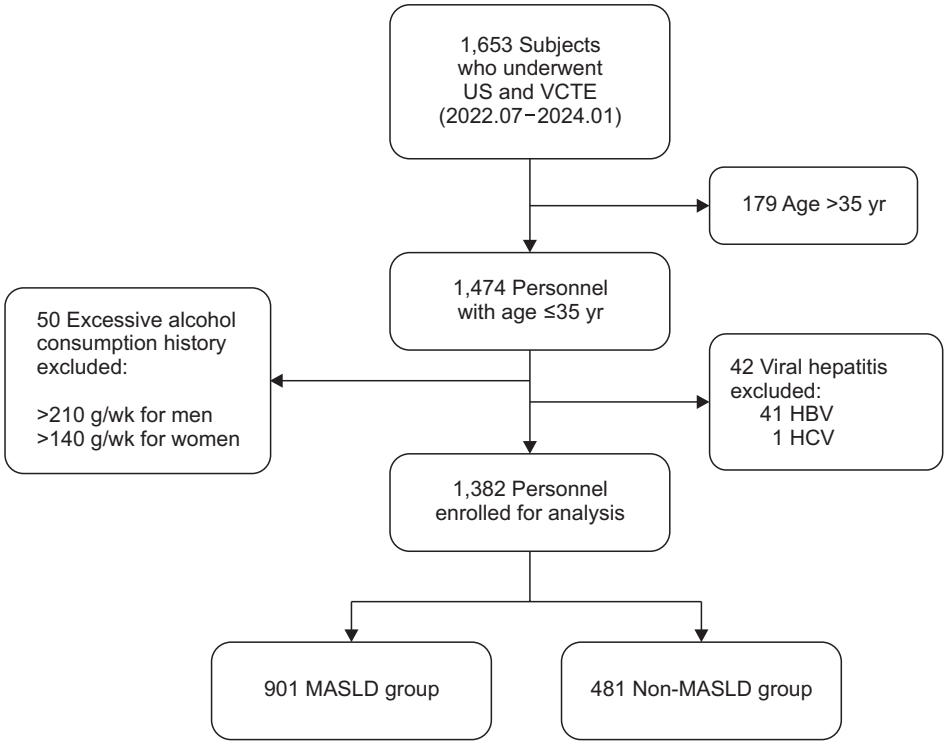

Fig. 1. Patient selection flowchart. US, ultrasound; VCTE, vibration-controlled transient elastography; HBV, hepatitis B virus; HCV, hepatitis C virus; MASLD, metabolic dysfunction-associated steatotic liver disease.

Table 1. Baseline Characteristics

Characteristic	Total (n=1,382)	No MASLD (n=481)	MASLD (n=901)	p-value
Male sex	1,355 (98.0)	458 (95.2)	897 (99.6)	<0.001
Age, yr	23.3±5.0	22.9±4.6	23.5±5.2	0.024
BMI, kg/m^2	27.8±4.5	24.1±2.9	29.8±3.9	<0.001
WC, cm	94.2±13.2	83.4±8.7	100.0±11.3	<0.001
DM	67 (4.9)	11 (2.3)	56 (6.2)	0.002
HTN	207 (15.0)	55 (11.4)	152 (16.9)	0.009
Dyslipidemia	474 (34.3)	86 (17.9)	388 (43.1)	<0.001
WBC, ×10^3/μL	7.0±1.8	6.4±1.6	7.4±1.8	<0.001
PLT, ×10^3/μL	269.0±53.2	256.0±52.2	276.0±52.4	<0.001
CRP, mg/dL	0.3±0.5	0.2±0.5	0.3±0.5	<0.001
TB, mg/dL	0.9±0.4	1.0±0.5	0.9±0.4	0.088
AST, IU/L	37.5±25.6	25.0±12.9	44.2±28.1	<0.001
ALT, IU/L	69.2±59.8	33.6±29.9	88.3±63.0	<0.001
GGT, U/L	55.1±46.2	36.0±39.2	65.2±46.4	<0.001
Albumin, mg/dL	4.9±0.3	4.9±0.3	5.0±0.3	<0.001
PT, INR	1.0±0.1	1.0±0.1	1.0±0.1	<0.001
Triglycerides, mg/dL	146.1±119.0	96.4±56.1	172.1±134.1	<0.001
HDL, mg/dL	52.8±13.2	59.8±14.2	49.1±10.9	<0.001
LSM, kPa	5.4±2.1	4.5±1.0	5.9±2.3	<0.001
LSM ≥10 kPa	48 (3.5)	0	48 (5.3)	<0.001
CAP, dB/m	281.6±63.9	210.0±30.8	319.9±39.5	<0.001
Probes				<0.001
M	1,046 (75.7)	461 (95.8)	585 (64.9)	
XL	336 (24.3)	20 (4.2)	316 (35.1)	

Data are presented as number (%) or mean±SD.
MASLD, metabolic dysfunction-associated steatotic liver disease; BMI, body mass index; WC, waist circumference; DM, diabetes mellitus; HTN, hypertension; WBC, white blood cell; PLT, platelet; CRP, C-reactive protein; TB, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; PT, prothrombin time; INR, international normalized ratio; HDL, high-density lipoprotein; LSM, liver stiffness measurement; CAP, controlled attenuation parameter.

dyslipidemia (43.1% vs 17.9%, p<0.001) than the non-MASLD group. Laboratory findings indicative of inflammation and liver function, such as white blood cell count, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase levels, were higher in the MASLD group than in the non-MASLD group. In terms of the CAP score, the MASLD group had a mean value of 319.9 dB/m, whereas the non-MASLD group had a value of 210.0 dB/m (p<0.001).

2. Steatosis indices depending on the presence of MASLD and degree of steatosis

Eight steatosis indices were calculated and compared between MASLD and non-MASLD groups. All indices showed statistically significant differences between the MASLD and non-MASLD groups (Supplementary Table 2). Furthermore, within the MASLD group, steatosis indices were compared across different degrees of steatosis as determined by the CAP score (Fig. 2). In terms of HSI and FLI (Fig. 2A and B), both indices exhibited significant differences between S1 and S2 (HSI: 41.7 vs 45.8, p<0.001; FLI: 58.3 vs 73.4, p<0.001) and between S2 and S3 (HSI: 45.8 vs 47.8, p<0.001; FLI: 73.4 vs 79.9, p<0.001). Other indices, including FSI, DSI, ZJU, LAP, and TyG-BMI (Fig. 2C-H) also showed significant differences between S1, S2, and S3. While VAI displayed significant differences between S2 and S3 (2.08 vs 2.62, p=0.003), no statistically significant difference was noted between S1 and S2, with scores of 1.85 and 2.08, respectively (p=0.186) (Fig. 2G). When comparing S1 to S3, all indices exhibited significant differences.

3. Correlation between steatosis indices and CAP score

Each index, along with the CAP score, was assessed for correlation (Fig. 3). When the steatosis indices were evaluated for their correlations with the CAP score, all indices except LAP and VAI exhibited strong correlations (r>0.6). ZJU displayed the strongest correlation coefficient (r=0.74), followed by FLI (r=0.73), HSI (r=0.71), and DSI (r=0.71). LAP showed a correlation coefficient of 0.48, indicating a moderate correlation with the CAP score, whereas VAI exhibited a weak correlation, with an r-value of 0.34. Furthermore, when steatosis indices were assessed for their correlation with the FLI, all indices, except VAI (r=0.50), demonstrated strong correlations with the FLI.

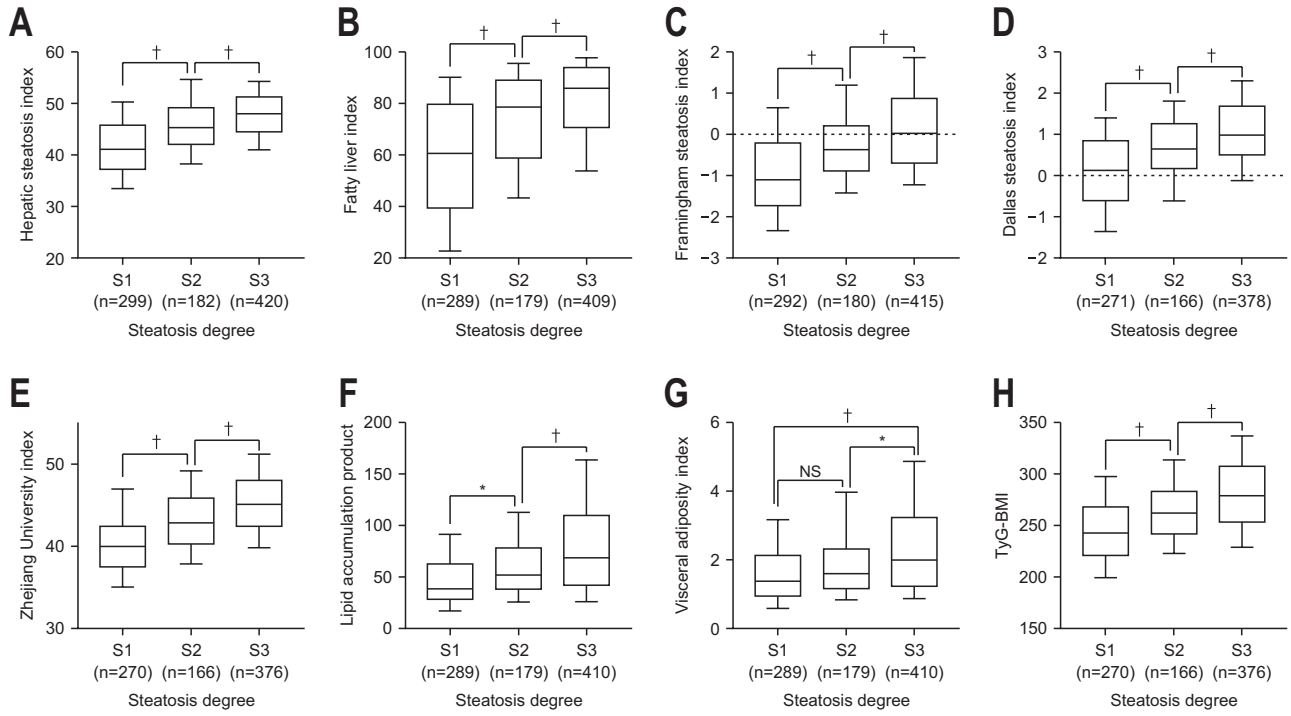

Fig. 2. Boxplot of steatosis indices stratified by steatosis severity. (A) Hepatic steatosis index. (B) Fatty liver index. (C) Framingham steatosis index. (D) Dallas steatosis index. (E) Zhejiang University index. (F) Lipid accumulation product. (G) Visceral adiposity index. (H) Triglyceride glucose-body mass index (TyG-BMI). All indices are significantly different between S1 and S3. NS, not significant. *p<0.01, †p<0.001.

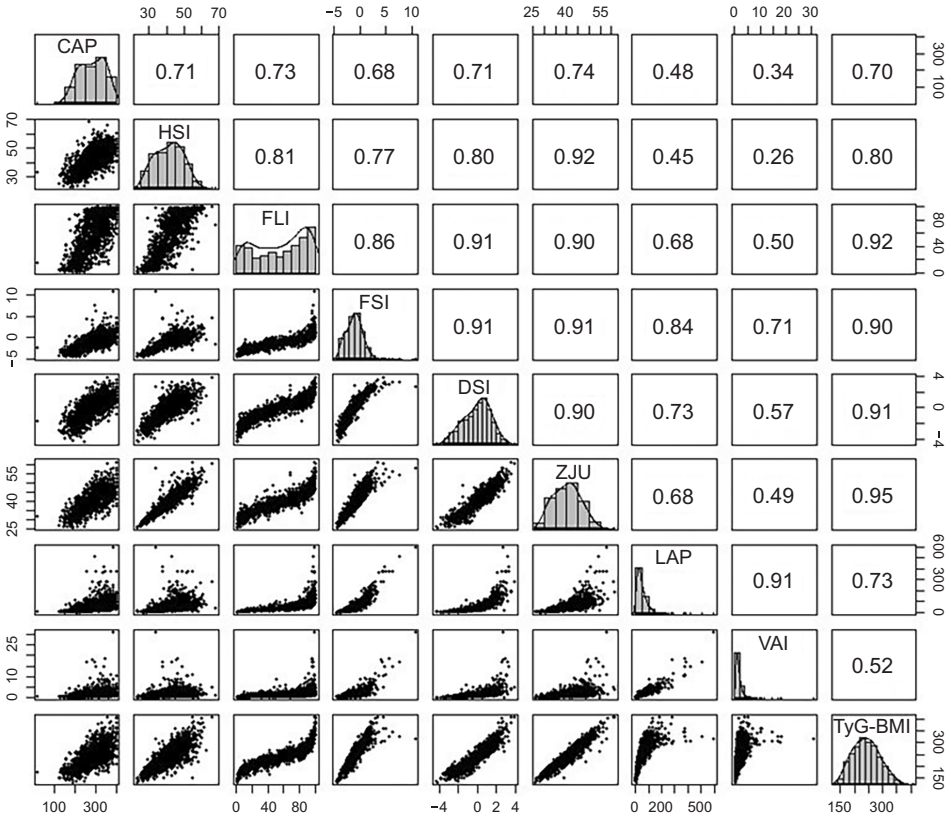

Fig. 3. Scatterplot depicting correlations between steatosis indices and controlled attenuation parameter (CAP) score. Upper panel shows correlation coefficients (r) between two associated parameters. HSI, hepatic steatosis index; FLI, fatty liver index; FSI, Framingham steatosis index; DSI, Dallas steatosis index; ZJU, Zhejiang University index; LAP, lipid accumulation product; VAI, visceral adiposity index; TyG-BMI, triglyceride glucose-body mass index.

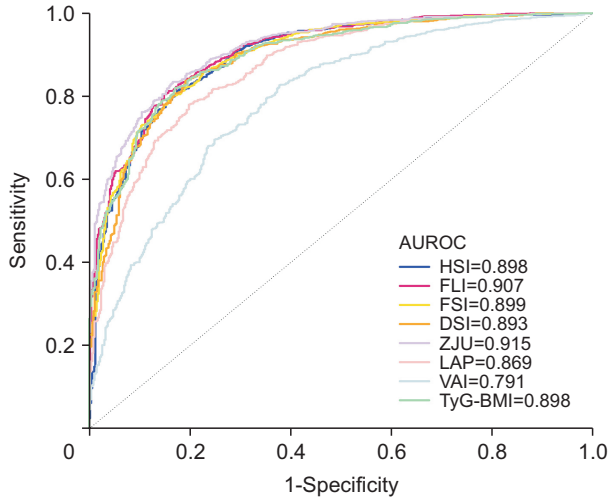

Fig. 4. Area under the receiver operating characteristic curve (AUROC) of steatosis indices for the diagnosis of metabolic dysfunction-associated steatotic liver disease. HSI, hepatic steatosis index; FLI, fatty liver index; FSI, Framingham steatosis index; DSI, Dallas steatosis index; ZJU, Zhejiang University index; LAP, lipid accumulation product; VAI, visceral adiposity index; TyG-BMI, triglyceride glucose-body mass index.

4. Comparison of predictive performance between steatosis indices

All steatosis indices were assessed for their predictive performance in identifying MASLD. Fig. 4 shows the AUROC of each index for predicting MASLD. HSI and FLI demonstrated AUROC values of 0.898 (95% confidence interval [CI], 0.881 to 0.915) and 0.907 (95% CI, 0.891 to 0.923), respectively. AUROC of other indices including FSI (0.899; 95% CI, 0.883 to 0.917), DSI (0.893; 95% CI, 0.875 to 0.911), ZJU (0.915; 95% CI, 0.900 to 0.931), LAP (0.869; 95% CI, 0.849 to 0.889), and TyG-BMI (0.898; 95% CI, 0.880 to 0.915) all exhibited good to excellent accuracy in predicting MASLD. However, VAI showed an AUROC of 0.791 (95% CI, 0.766 to 0.817), indicating fair accuracy in predicting MASLD.

Additionally, each steatosis index was compared to the FLI, the most widely used steatosis index, for predictive performance (Supplementary Table 3). The HSI, FSI, DSI, ZJU, and TyG-BMI were not significantly different from the FLI in terms of predictive performance. In contrast, LAP and VAI were statistically inferior to FLI, with p-values of 0.003 and <0.001, respectively. Calibration plots for the steatosis indices are shown in Supplementary Fig. 1.

Furthermore, steatosis indices were assessed for their predictive value in discriminating hepatic steatosis, defined as a CAP score of ≥250 dB/m, showing a predictive performance similar to that observed for MASLD (Supplementary Fig. 2). The performance of steatosis indices based on the probes used (M probe or XL probe) is depicted in Supplementary Fig. 3.

5. Comparison of predictive performance in differentiating various degrees of steatosis

Eight steatosis indices were evaluated for their ability to differentiate between various grades of steatosis in patients with MASLD. Supplementary Fig. 4 illustrates the AUROC values representing the predictive performance of these indices for distinguishing S2 or S3. In differentiating steatosis grade S2 or higher from S1, HSI (AUROC, 0.751; 95% CI, 0.716 to 0.786), FLI (AUROC, 0.737; 95% CI, 0.702 to 0.772), FSI (AUROC, 0.726; 95% CI, 0.690 to 0.762), DSI (AUROC, 0.723; 95% CI, 0.685 to 0.761), ZJU (AUROC, 0.755; 95% CI, 0.718 to 0.791), and TyG-BMI (AUROC, 0.714; 95% CI, 0.676 to 0.752) demonstrated fair performance as shown in Supplementary Fig. 4A. For distinguishing S3 from S1 or S2, HSI (AUROC, 0.717; 95% CI, 0.684 to 0.751), FLI (AUROC, 0.703; 95% CI, 0.669 to 0.737), DSI (AUROC, 0.700; 95% CI, 0.665 to 0.736), and ZJU (AUROC, 0.729; 95% CI, 0.695 to 0.764) demonstrated fair performance, while the remaining indices showed AUROC values below 0.7 (Supplementary Fig. 4B).

6. Sensitivity analysis of predictive performance using ultrasound as a determinant

Sensitivity analysis was conducted using ultrasound as a determinant of hepatic steatosis to evaluate the predictive performance of the steatosis indices (Supplementary Fig. 5). The AUROC of each steatosis index demonstrated values similar to those of the previous results, which utilized a CAP score ≥250 dB/m as the definition for steatosis. In this assessment, all indices exhibited good to excellent accuracy in predicting MASLD, except for the VAI, which showed an AUROC of 0.793, indicating fair accuracy.

7. Threshold for HSI and FLI for determining MASLD in young adults

The two most used indices, the FLI and HSI, were evaluated for their appropriate cutoff values for defining MASLD in young adults. Table 2 presents the range of FLI and HSI values along with corresponding performance metrics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive likelihood ratio, and negative likelihood ratio.

For the FLI, a score of 30 was used as the rule-out cutoff, and a score of 60 was used as the rule-in cutoff in the original study. In our study cohort, an FLI value of 30 demonstrated a sensitivity of 93.3%, specificity of 66.5%, and NPV of 83.8%, validating its adequacy as a cutoff for ruling out MASLD in this population. Additionally, an FLI of 60 exhibited a specificity of 89.1%, sensitivity of 71.7%,

Table 2. Thresholds for FLI and HSI and Their Corresponding Diagnostic Performance

	Thresholds	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %	LR+	LR–
FLI	≥30	93.3	66.5	84.2	83.8	84.1	2.8	0.1
	≥35	90.4	71.3	85.8	79.5	83.9	3.1	0.1
	≥40	87.5	76.2	87.6	76.0	83.6	3.7	0.2
	≥45	83.5	81.4	89.6	72.0	82.8	4.5	0.2
	≥50	79.7	85.1	91.1	68.6	81.6	5.4	0.2
	≥55	76.3	87.5	92.2	65.8	80.1	6.1	0.3
	≥60	71.7	89.1	92.6	62.1	77.7	6.6	0.3
	≥65	66.4	91.0	93.4	58.5	74.8	7.4	0.4
HSI	≥30	99.3	24.8	71.3	95.2	73.4	1.3	0.0
	≥32	98.0	39.1	75.1	91.7	77.6	1.6	0.1
	≥34	95.9	55.2	80.1	87.8	81.8	2.1	0.1
	≥36	92.3	67.7	84.3	82.5	83.8	2.9	0.1
	≥38	85.6	76.0	87.0	73.7	82.3	3.6	0.2
	≥40	79.6	83.5	90.1	68.6	80.9	4.8	0.2
	≥42	70.5	89.6	92.7	61.8	77.1	6.8	0.3

FLI, fatty liver index; HIS, hepatic steatosis index; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR–, negative likelihood ratio.

and PPV of 92.6%, demonstrating its adequacy as a cutoff for ruling in MASLD.

Regarding the HSI, the original study defined a value of 30 as the rule-out cutoff and 36 as the rule-in cutoff for NAFLD. However, in our study cohort, an HSI of 36 displayed inadequate specificity for ruling in criteria, with a specificity and NPV of 67.7% and 84.3%, respectively. Moreover, an HSI of 30 exhibited very low specificity (24.8%) and relatively low accuracy (73.4%) compared to the other values, with a sum of sensitivity and specificity of less than 150%. Hence, an alternative threshold was necessary for our study cohort. In this context, an HSI value of 42 demonstrated adequate performance as a rule-in cutoff, with a specificity of 89.6%, sensitivity of 70.5%, and PPV of 92.7%. For the rule-out cutoff, an HSI of 36 showed a sensitivity of 92.3% and NPV of 82.5%, while maintaining acceptable specificity (67.6%), thus proving to be an adequate threshold in this specific population.

DISCUSSION

In our comprehensive analysis, we evaluated the predictive performance of eight steatosis indices, namely, the HSI, FLI, FSI, DSI, ZJU, LAP, VAI, and TyG-BMI, for MASLD in young adults under 35 years of age. Most steatosis indices achieved AUROC values exceeding 0.8, indicating good to excellent performance in predicting MASLD, whereas the VAI exhibited an AUROC of 0.791, demonstrating fair performance in predicting MASLD. When comparing the predictive performance of steatosis indices to that of the FLI, the most widely used steatosis index, LAP and VAI showed inferior outcomes ($p=0.003$ and $p<0.001$, respectively), whereas other indices were found to be noninferior. Our study also validated the ability to discriminate between steatosis severities, revealing significant differences in the values of these indices according to steatosis severity. To the best of our knowledge, this is the first study to investigate the performance of these indices in a specific age group (<35 years).

Many studies have attempted to validate these indices in discriminating NAFLD across diverse ethnicities.[30-33] Although these indices have generally demonstrated acceptable results in validation sets, there have been reports indicating variations in performance among these indices.[11,12,34,35] In a recent study by Zou *et al.*,[12] the performance of the VAI exhibited significant inferiority compared to the HSI, FLI, FSI, ZJU, and TyG-BMI. Additionally, LAP also demonstrated inferior results compared to FLI, consistent with our findings of inferior outcomes for VAI and LAP. While other steatosis indices are primarily derived for diagnosing NAFLD within populations, VAI and LAP are designed for other purposes, such as assessing cardiometabolic risk and metabolic syndrome. The relatively inferior performance of these two biomarkers can be understood by considering the fundamental differences in their development.

Our study evaluated the cutoff values of the two most widely used indices, the FLI and HSI, in this young population. For FLI, the proposed cutoff values of <30 for ruling out NAFLD and ≥60 for ruling in NAFLD proved to be adequate for defining MASLD in the young adult population. However, the HSI yielded different results with respect to the original cutoff values. The original ruling in cutoff value of 36 exhibited a specificity below the acceptable range, measuring only 67.7%. Consequently, our study proposed

new cutoff values specifically tailored for young adults, suggesting <36 for ruling out MASLD and ≥42 for ruling in MASLD. The discrepancy between these two indices can be explained by the different compositions of each formula and the distinct demographics of the MASLD in the young age group. Demographics of MASLD can differ between age groups, and young patients with MASLD have been recognized for their relatively higher probability of obesity compared to other age groups.[15] Additionally, in the context of the morbidly obese population, a recent report suggested a higher cutoff value of HSI for defining moderate hepatic steatosis.[36] Taking into account the higher proportion of obesity among young adults with MASLD, it is understandable that HSI values in this population are higher, given that BMI constitutes a significant portion of the HSI formula.

Our results have several important implications for the field of MASLD diagnosis. Given the fact that the prevalence of MASLD has substantially increased in recent years in young age groups, active screening for young adults to determine the presence of MASLD is mandatory in current society to lighten the socioeconomic burden in the near future.[4] As our study is the first to validate noninvasive indices for discriminating MASLD in young adults group, the findings of our study could contribute to the early diagnosis of MASLD, followed by tailored intervention to prevent disease progression, thus resulting in the regression of disease burden caused by MASLD. Furthermore, with the escalating economic burden confronting patients with MASLD, there is a growing imperative for the effective allocation of resources.[37,38] Within this framework, proposing revised cutoff values for the widely used HSI holds promise for enhancing the accuracy of MASLD screening. This refinement has the potential to facilitate targeted management strategies and ensure the optimal distribution of financial resources to individuals genuinely at risk of MASLD.

The present study has several limitations. First, it was conducted at a single center with a relatively homogeneous ethnicity, which may impede the generalizability of the study results. Moreover, as the characteristics of MASLD can vary among different ethnicities, further validation in diverse ethnic groups is warranted.[39] Additionally, the study used the CAP score for diagnosing hepatic steatosis instead of liver biopsy, which is considered the gold standard for such diagnosis. While the CAP score has demonstrated a high predictive value for hepatic steatosis, the use of the gold standard method could have enhanced the reliability of the results.[40] Further research employing liver biopsy or magnetic resonance imaging-proton density fat fraction is needed to better assess the diagnostic performance of steatosis indices. Lastly, the sex distribution of the study cohort was skewed towards male populations, necessitating further validation in the female population. Despite these limitations, we believe that our study contributes to a deeper understanding of the characteristics of young patients with MASLD by validating established steatosis indices and proposing new cutoff values tailored to this demographic.

In conclusion, our findings suggest that the established steatosis indices apply even in younger age groups, with new cutoff values for HSI proposed for the young population. These findings are anticipated to inform future studies on young adults with MASLD and may help mitigate potential biases arising from inappropriate cutoff values.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Study concept and design: J.L., H.Y. Data collection: J.L., C.I.H. Data analysis and interpretation: J.L., D.Y.L., H.Y. Drafting of the manuscript: J.L., H.Y. Conceptualization, methodology, and supervision: J.L., P.S.S., S.H.B., H.Y. Approval of final manuscript: all authors.

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at https://doi.org/10.5009/gnl240323.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplemental material. Further in-

quiries can be directed at the corresponding author.

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