



Research article

Comparing non-alcoholic fatty liver disease indices in predicting the prevalence and incidence of metabolic syndrome in middle-aged adults

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ARTICLE INFO

Keywords:

Metabolic syndrome
Non-alcoholic fatty liver disease
Fatty liver index
Hepatic steatosis index
Risk assessment

ABSTRACT

Aims: This study aimed to compare the predictive power of the indices of non-alcoholic fatty liver disease (NAFLD), the fatty liver index (FLI), and the hepatic steatosis index (HSI) for the prevalence and incidence of metabolic syndrome (MetS) in a community-based prospective cohort over a 16-year follow-up period.

Methods: Data from the Ansan-Ansung cohort of the Korean Genome and Epidemiology Study were used. We evaluated 8271 participants for MetS prevalence and 5242 participants without MetS at baseline for MetS incidence.

Results: The baseline prevalence of MetS was 30.5 %. The FLI and HSI were significantly associated with MetS prevalence, with the FLI showing superior predictive ability compared with the HSI. During the 16-year follow-up period, 2286 participants (43.6 %) developed MetS. Both indices were significantly associated with the incidence of MetS. Time-dependent receiver operating characteristic curve analysis, Harrell's C-index, and integrated discrimination improvement indicated that the FLI demonstrated better predictive power for MetS incidence than the HSI.

Conclusions: Given the increasing prevalence of MetS and its health implications, incorporating the FLI into clinical practice can improve early detection and intervention strategies. Future research should investigate the applicability of the FLI in diverse populations and its role in comprehensive MetS management protocols.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by an increased liver fat content of over 5 % in the absence of significant

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alcohol consumption or other secondary causes of steatosis. This is the most common chronic liver disease globally, and its prevalence is rapidly increasing [1–3]. Although NAFLD can progress to cirrhosis and hepatocellular carcinoma, cardiometabolic complications are the primary causes of morbidity and mortality [4,5]. NAFLD is commonly associated with metabolic risk factors and is considered a hepatic manifestation of metabolic syndrome (MetS) [5,6], which is characterized by a cluster of metabolic disorders, including abdominal obesity, hypertension, dyslipidemia, and impaired glycemia [7]. Regardless of the cause or consequence of MetS, NAFLD often co-occurs with MetS and its components [8,9]. Research has demonstrated that MetS is associated with cardiometabolic diseases, cancer, and increased mortality [10,11]. Consequently, the early detection of MetS is crucial in clinical settings, as it encourages healthcare professionals to search for its numerous associated conditions and paves the way for preventing its complications through pharmaceutical and non-pharmaceutical interventions.

For mass screening a target population, it is important to have simple, noninvasive, and inexpensive tests. For example, while the gold standard test for diagnosing NAFLD is a liver biopsy, this procedure has limitations related to invasiveness [12]. Conventional radiological imaging studies, such as ultrasonography, computed tomography, and magnetic resonance imaging, are reasonably accurate but are too expensive for mass screening tests [12]. For these reasons, simple and noninvasive indices are widely used for large-scale screening and population studies of NAFLD. The FLI and HSI are validated indices widely used for diagnosing NAFLD [13, 14]. Although NAFLD is closely associated with MetS [15], it remains unclear which surrogate markers for diagnosing NAFLD are more suitable for predicting the prevalence and incidence of MetS. Therefore, this study aimed to compare the predictive power of the FLI and HSI for the prevalence and incidence of MetS in middle-aged Korean adults using a large community-based cohort over a follow-up period of 16 years.

2. Materials and methods

2.1. Study participants

We utilized data from the Ansan–Ansung cohort, part of the Korean Genome and Epidemiology Study, which included 10,030 South Koreans aged 40–69 years from the cities of Ansong and Ansan. Initiated in 2001, this government-funded cohort study aimed to investigate the genetic and environmental factors contributing to common metabolic and cardiovascular diseases. Detailed methodologies for the Ansan–Ansung cohort have been published previously [16,17]. In summary, the participants underwent comprehensive health examinations at a regional tertiary hospital, including demographic, social, and medical histories, physical examinations, laboratory tests for blood and urine, electrocardiography, and chest radiography. This study incorporated eight sequential follow-up evaluations conducted biennially until 2018 in accordance with the cohort protocol.

From the baseline participants of 10,030, we selected 8271 suitable participants to evaluate the prevalence of MetS according to the NAFLD indices. A total of 1759 participants were excluded from the analysis, including 372 individuals with missing values required for calculating MetS components or NAFLD indices (FLI and HSI), 423 individuals with a history of viral hepatitis, and 964 individuals who were heavy alcohol consumers (>30 g/day for men and >20 g/day for women). Viral hepatitis and heavy alcohol consumption were exclusion criteria for NAFLD because they could influence the NAFLD indices.

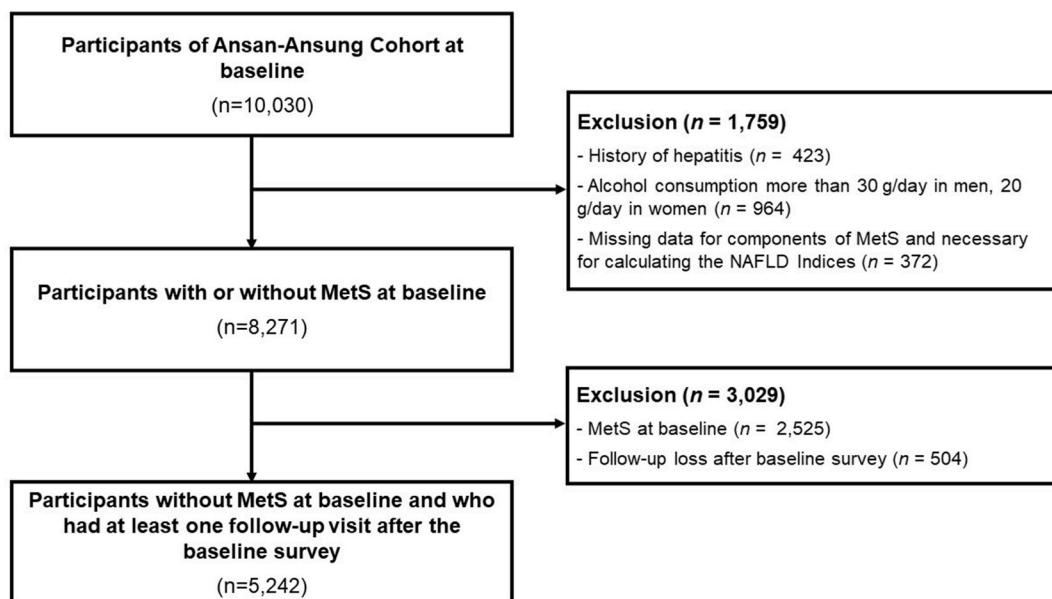


Fig. 1. Study flowchart.

MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease.

In addition, to compare the predictive power of the FLI and HSI for the incidence of MetS, we analyzed data from 5242 participants without MetS at baseline, excluding those with baseline MetS ($n = 2525$) and those without follow-up data after the baseline survey ($n = 504$) from 8271 participants (Fig. 1).

2.2. Data collection

Demographic, social, and medical history information, such as smoking status, alcohol consumption, education, income level, marital status, medical conditions (including hypertension, diabetes mellitus, dyslipidemia, and chronic kidney disease), and history of cardiovascular disease (defined as a composite of ischemic heart disease, hemorrhagic stroke, ischemic stroke, heart failure, and peripheral artery disease) were obtained using a questionnaire administered by trained investigators at a tertiary hospital. Additionally, the questionnaire collected data on physical activity, including regular exercise, types of exercise, weekly exercise frequency and duration, and daily physical activity and duration. The total physical activity per week was calculated by adding the metabolic equivalent task scores of the exercises and routine physical activity.

We defined hypertension as a systolic blood pressure (SBP) of 140 mmHg or higher, a diastolic blood pressure (DBP) of 90 mmHg or higher, or the use of antihypertensive medications [18]. Diabetes mellitus was defined as a fasting blood glucose level of 126 mg/dL or higher, a hemoglobin A1c level of 6.5 % or higher, or the use of antidiabetic medications [19]. Furthermore, we defined dyslipidemia as a total cholesterol level of 240 mg/dL or higher, low-density lipoprotein (LDL) cholesterol level of 160 mg/dL or higher, triglyceride (TG) level of 200 mg/dL or higher, high-density lipoprotein (HDL) cholesterol level of less than 40 mg/dL in men or less than 50 mg/dL in women, or the use of lipid-lowering medications [20].

The participants' blood pressure (BP) was measured by trained examiners using a mercury sphygmomanometer at the heart level while in a sitting position after at least 5 min of rest. At least two BP readings were taken at intervals of at least 1 min, and the average was recorded. Blood samples were collected after overnight fasting and analyzed using an automated analyzer (Hitachi Automatic Analyzer 7600; Hitachi, Tokyo, Japan). Fasting blood glucose, serum insulin, HDL cholesterol, TG, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and hemoglobin A1c levels were measured. LDL cholesterol was calculated using the Friedewald equation when the TG levels were below 400 mg/dL [21]. The Modification of Diet in Renal Disease equation was used to calculate the estimated glomerular filtration rate [22].

2.3. MeS definition

MetS was defined using harmonized worldwide consensus criteria developed by major organizations, including the International Diabetes Federation, the National Heart, Lung, and Blood Institute, and the American Heart Association, which were based on and extended the National Cholesterol Education Program Adult Treatment Panel III criteria. MetS was diagnosed when at least three of the five components were present [23]. These components are (1) abdominal obesity, defined as a waist circumference (WC) greater than 90 cm in men and greater than 85 cm in women according to the Korean Society of Obesity, (2) hypertriglyceridemia, with serum TG ≥ 150 mg/dL, (3) low HDL-C, with serum HDL-C < 40 mg/dL in men or < 50 mg/dL in women, (4) hypertension, with SBP ≥ 130 mmHg, DBP ≥ 85 mmHg, or treatment with antihypertensive drugs, (5) high fasting blood glucose, with fasting serum glucose > 100 mg/dL, a previous diagnosis of type 2 diabetes mellitus, a prescription of medications for diabetes mellitus [23–25].

2.4. NAFLD indices calculation

The FLI and HSI indices were selected based on recommendations from the Korean Association for the Study of the Liver (KASL) clinical practice guidelines [26]. The FLI, which incorporates body mass index (BMI), WC, TG, and GGT levels, is a clinically validated tool for identifying hepatic steatosis [13]. The formula for FLI is as follows: $FLI = (e^{0.953 \times \log_e(TG)} + 0.139 \times BMI + 0.718 \times \log_e(GGT) + 0.053 \times WC - 15.745) / (1 + e^{0.953 \times \log_e(TG)} + 0.139 \times BMI + 0.718 \times \log_e(GGT) + 0.053 \times WC - 15.745)} \times 100$.

The formula for the HSI, another validated index for detecting NAFLD, is $8 \times ALT/AST + BMI$. Two additional points were given if the patient had diabetes mellitus or was female [14]. The FLI can exclude NAFLD when it is less than 30 and diagnose NAFLD when it is 60 or greater. The thresholds for excluding or diagnosing NAFLD with the HSI are 30 or less and 36 or greater, respectively [13,14].

2.5. Statistical analysis

The baseline characteristics of the 8271 participants were compared and stratified by the presence or absence of MetS at baseline. Categorical variables are presented as numbers and percentages, whereas continuous variables are reported as means with standard deviations (SD) or medians with interquartile ranges, depending on their distribution. Continuous variables were compared using either the Student's *t*-test or the Mann–Whitney *U* test, depending on their distribution, and assessed using the Kolmogorov–Smirnov test and visual inspection of Q–Q plots. Categorical variables were compared using the chi-square test or Fisher's exact test.

To evaluate and compare the predictive abilities of the NAFLD indices for prevalent MetS, the area under the receiver operating characteristic (ROC) curves (AUCs) was calculated for the 8271 participants at baseline. Additionally, logistic regression analyses were conducted to explore the association between MetS prevalence and each NAFLD index after adjusting for potential confounding variables. Clinically relevant metabolic risk factors were chosen as confounders, and adjusted models were developed as follows: Model 1 was adjusted for age (per 1 year) and sex. Model 2 included variables from Model 1 alongside sociodemographic factors, encompassing BMI, smoking status, alcohol consumption, physical activity (per 1 metabolic equivalent task-hour/week), income level,

and education. Furthermore, Model 3 integrated comorbid conditions associated with MetS (hypertension, diabetes mellitus, and dyslipidemia) in addition to the variables from Model 2. Reduced models were constructed through a backward elimination procedure using the best Akaike's information criterion. The analysis was performed using the NAFLD index as a continuous variable, as well as utilizing their threshold value of the NAFLD index.

For participants without MetS at baseline, the independent predictive significance of each NAFLD index for incident MetS during follow-up was assessed using the Cox proportional hazards regression model, accounting for potential confounders. The same models as previously described were used in the multivariable analysis. Additionally, we evaluated and compared the predictive ability of the NAFLD indices using a time-dependent ROC curve for the 10-, 12-, 14-, and 16-year incidences of MetS during the follow-up period. Beyond the time-dependent ROC curve analysis, we also used Harrell's C-index, net reclassification index (NRI), and integrated discrimination index (IDI) to compare the predictive abilities of the NAFLD indices for MetS incidence. Calibration analyses were

Table 1
Baseline characteristics of the participants with or without MetS.

	Overall n = 8271	Without MetS at baseline n = 5746	With MetS at baseline n = 2525	p-value
Age, years	52.38 ± 8.90	51.06 ± 8.74	55.36 ± 8.55	<0.001
Men, n (%)	3440 (41.6)	2539 (44.2)	901 (35.7)	<0.001
BMI, kg/m ²	24.54 ± 3.14	23.67 ± 2.83	26.52 ± 2.93	<0.001
Waist circumference, cm	82.65 ± 8.90	79.60 ± 7.68	89.60 ± 7.45	<0.001
Income level, n (%)				<0.001
> = Median	3859 (47.6)	2916 (51.7)	943 (38.2)	
Education, n (%)				<0.001
Lower than middle school	2842 (34.7)	1652 (29.0)	1190 (47.7)	
Middle school	1883 (23.0)	1362 (23.9)	521 (20.9)	
High school	2453 (29.9)	1904 (33.4)	549 (22.0)	
University and college	1019 (12.4)	786 (13.8)	233 (9.3)	
Smoking status, n (%)				<0.001
Current smoker	1794 (22.0)	1317 (23.2)	477 (19.2)	
Ex-smoker	1135 (13.9)	798 (14.1)	337 (13.5)	
Never-smoker	5224 (64.1)	3550 (62.7)	1674 (67.3)	
Alcohol consumption, n (%)				<0.001
Current drinker	3395 (41.4)	2544 (44.6)	851 (34.1)	
Ex-drinker	571 (7.0)	373 (6.5)	198 (7.9)	
Never-drinker	4227 (51.6)	2783 (48.8)	1444 (57.9)	
Physical activity, METs-hour/week	170.89 ± 104.11	170.69 ± 101.93	171.36 ± 108.92	0.79
Systolic blood pressure, mmHg	124.15 ± 18.81	119.37 ± 17.22	135.03 ± 17.71	<0.001
Diastolic blood pressure, mmHg	81.28 ± 11.72	78.49 ± 10.97	87.61 ± 10.87	<0.001
Medical history, n (%)				
Hypertension	942 (11.4)	304 (5.3)	638 (25.3)	<0.001
Diabetes mellitus	185 (2.2)	35 (0.6)	150 (5.9)	<0.001
Dyslipidemia	43 (0.5)	23 (0.4)	20 (0.8)	0.035
Chronic kidney disease	239 (2.9)	143 (2.5)	96 (3.8)	0.001
Laboratory data				
eGFR, mL/min/1.73m ²	89.74 ± 20.24	90.66 ± 19.99	87.67 ± 20.65	<0.001
Fasting glucose, mg/dL	82 (77, 89)	82 (77, 87)	85 (79, 98)	<0.001 ^a
Hemoglobin A1c, %	5.6 (5.3, 5.9)	5.5 (5.3, 5.8)	5.8 (5.5, 6.2)	<0.001 ^a
Total cholesterol, mg/dL	189 (167, 213)	185 (164, 210)	196 (175, 221)	<0.001 ^a
Triglyceride, mg/dL	133 (98, 185)	115 (90, 145)	192 (155, 255)	<0.001 ^a
HDL cholesterol, mg/dL	43 (37, 50)	46 (40, 52)	38 (34, 44)	<0.001 ^a
LDL cholesterol, mg/dL	122 (102, 144)	118 (99, 141)	128 (109, 150)	<0.001 ^a
ALT, IU/L	22 (17, 30)	21 (16, 28)	25 (19, 35)	<0.001 ^a
AST, IU/L	26 (22, 31)	26 (22, 30)	27 (23, 32)	<0.001 ^a
GGT, IU/L	17 (12, 30)	15 (11, 27)	22 (14, 39)	<0.001 ^a
NAFLD indices				
Fatty liver index	24.05 (10.82, 46.09)	15.77 (8.07, 30.69)	49.89 (32.59, 67.74)	<0.001 ^a
Hepatic steatosis index	32.71 (29.94, 35.84)	31.52 (29.08, 34.18)	35.70 (33.10, 38.59)	<0.001 ^a
MetS component (%)				<0.001
Score 0	1356 (16.4)	1356 (23.6)	0 (0.0)	
Score 1	2286 (27.6)	2286 (39.8)	0 (0.0)	
Score 2	2104 (25.4)	2104 (36.6)	0 (0.0)	
Score 3	1560 (18.9)	0 (0.0)	1560 (61.8)	
Score 4	818 (9.9)	0 (0.0)	818 (32.4)	
Score 5	147 (1.8)	0 (0.0)	147 (5.8)	

Categorical variables were presented as number (%) and continuous variables were presented as mean ± standard deviation or median (interquartile range) as appropriate. MetS, metabolic syndrome; BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; NAFLD, non-alcoholic fatty liver disease; MET, metabolic equivalent.

^a Assessed by nonparametric test.

performed to evaluate the agreement between predicted and observed values for both the FLI and HSI models, using calibration curves with 1000 bootstrap repetitions.

All statistical analyses were conducted using the open-source statistical software R (version 4.4.0, www.R-project.org) and RStudio (version 2023.12.1, www.rstudio.com), along with statistical packages including tableone, pROC, timeROC, rms, survminer, and survival. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 8271 participants were analyzed based on the presence or absence of MetS at baseline (Table 1). The average age was 52 years, and 41.6 % of the patients were men. Participants with MetS at baseline were older (55.36 ± 8.55 vs. 51.06 ± 8.74 years), had a lower prevalence of being male sex (35.7 % vs. 44.2 %), had a higher BMI, WC, systolic and diastolic BPs, and a higher prevalence of hypertension, diabetes, and chronic kidney disease (all $p < 0.001$) than those without MeS at baseline. Additionally, those with MetS had more abnormal laboratory profiles, including higher fasting glucose, hemoglobin A1c, total cholesterol, TG, and lower HDL cholesterol levels (all $p < 0.001$) than those without MeS. The FLI and HSI were significantly higher in participants with MetS ($p < 0.001$ for both). Furthermore, participants with MetS had significantly lower incomes and educational levels ($p < 0.001$ for both).

3.2. Predictive power of NAFLD indices for MetS prevalence

Supplementary Table 1 shows the prevalence of MetS at baseline and the corresponding odds ratios (ORs) with 95 % confidence intervals (CIs) according to the NAFLD indices. The overall prevalence of MetS at baseline was 30.5 %, and higher values of both indices were associated with increased odds for the prevalence of MetS. After full adjustment, the adjusted OR for each 1-SD increment in the FLI was 6.104 (5.464–6.819). Participants with FLI values of 30–60 and ≥ 60 had significantly higher odds of MetS prevalence compared with those with an FLI < 30 , with ORs of 7.296 (5.721–9.306) and 39.850 (30.189–52.603) in the fully adjusted model, respectively. Similar trends were observed for the HSI. However, the FLI generally showed higher ORs than the HSI. The ROC curve analysis in Fig. 2 shows the AUCs for the FLI and HSI in predicting MetS prevalence. FLI demonstrated superior predictive ability with an AUC of 0.845 (0.837–0.854) compared with HSI, with an AUC of 0.771 (0.761–0.782), $p < 0.001$. In addition, the FLI and HSI were well-calibrated for the prediction of MetS prevalence (Supplementary Fig. 2).

3.3. Predictive power of NAFLD indices for MetS incidence

Among the 5242 participants without MetS at baseline, 2286 (43.6 %) developed MetS during the 16-year follow-up period (Supplementary Fig. 1). Table 2 presents the incidence of MetS and the corresponding hazard ratios (HRs) with 95 % CIs based on the FLI and HSI. For each 1-SD increment in the FLI, the adjusted HR was 1.707 (1.590–1.834) after full adjustment. Participants with FLI values of 30–60 and ≥ 60 had significantly higher incidences of MetS compared with those with an FLI < 30 , with HRs of 1.717

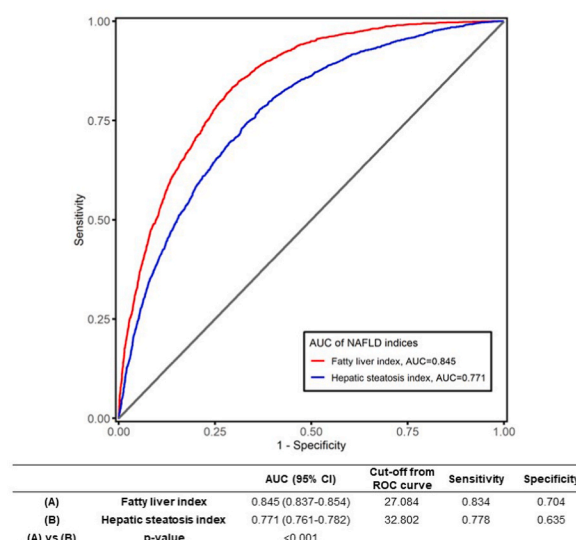


Fig. 2. Predictive ability of FLI and HSI for the prevalence of MetS using ROC curve analysis.

FLI, fatty liver index; HSI, hepatic steatosis index; MetS, metabolic syndrome; ROC, receiver operating characteristic; AUC, area under the ROC curve; NAFLD, nonalcoholic fatty liver disease; CI, confidence interval.

(1.531–1.926) and 2.177 (1.803–2.627), respectively. Similar trends were observed for the HSI, although the HRs were generally lower than those for the FLI. Time-dependent ROC curve analysis showed AUCs for the FLI and HSI in predicting the incidence of MetS over various periods (Fig. 3). The FLI demonstrated superior predictive ability, with 10-year, 12-year, 14-year, and 16-year AUCs ranging from 0.731 (0.716–0.745) to 0.718 (0.685–0.750), compared with HSI's AUCs ranging from 0.674 (0.658–0.690) to 0.689 (0.655–0.722). Except for the 16-year AUC, these differences were statistically significant. Harrell's C-index was also significantly higher for the FLI at 0.687 (0.676–0.697) compared with the HSI at 0.649 (0.637–0.660), indicating a better overall predictive performance. The IDI and NRI for reclassification using the FLI instead of the HSI were 0.027 (0.012–0.041), $p = 0.027$, and 0.047 (–0.003–0.093), $p = 0.08$, respectively (Table 3). In addition, the FLI and HSI were well-calibrated for the prediction of MetS incidence (Supplementary Fig. 3).

4. Discussion

This study aimed to compare the predictive power of the FLI and HSI for the prevalence and incidence of MetS in Korean adults using large-scale, community-based, prospective cohort data over 16 years. The FLI and HSI were significantly associated with the prevalence and incidence of MeS. The associations between each index and MetS were dose-dependent and significant, even when analyzed by applying known thresholds for diagnosing NAFLD, which is the inherent purpose of each index. In particular, the FLI showed better predictive power for the prevalence of MetS than the HSI, and this superiority was maintained across various periods of incidence, from 10 years to 16 years.

Previous studies have reported that NAFLD is a precursor to MetS. Robust evidence suggests that NAFLD and MetS share common risk factors and pathogenic mechanisms [27,28]. Both conditions are highly prevalent worldwide, and their prevalence is steadily increasing [29,30]. Given that cardiometabolic complications are the primary causes of morbidity and mortality in these diseases [4, 10], early detection of the transition from NAFLD to MetS is clinically important [15]. In a retrospective analysis of over 1 million young Koreans, the degree of hepatic steatosis evaluated using the FLI could predict future MetS occurrence [31]. The HSI also reported a relationship with MetS incidence in women in a relatively small prospective cohort study in Italy [32]. Our results are consistent with those of previous studies in terms of the association between the FLI and HSI and the incidence of MetS. In addition, our study adds new information in which the FLI showed better predictive power for the prevalence and incidence of MetS than the two representative NAFLD indices.

Although the precise mechanisms underlying the superiority of the FLI over the HSI for predicting MetS are not understood, several explanations have been suggested. The FLI and HSI share the common feature of being easily computed from readily measurable components. However, the distinct composition of each index may account for the differences in their predictive abilities. First, the FLI includes WC and BMI, whereas the HSI considers only BMI. WC is a more reliable indicator of obesity-related health risks and insulin resistance than BMI alone because it better reflects visceral fat accumulation, which is closely linked to the metabolic dysfunction associated with MetS [33,34]. Second, the FLI incorporates TG, a key marker of lipid metabolism abnormalities, which are components of MetS and are significant risk factors for cardiovascular disease [35]. In contrast, the HSI does not directly include factors related to lipid metabolism. TG is associated with insulin resistance and is a component of the TG and glucose index and the metabolic score for insulin resistance index, which are known indicators of insulin resistance [36]. Therefore, the FLI provides a more comprehensive assessment of the cardiometabolic risks that underlie MetS. These hypotheses may help explain why the FLI has a better predictive performance for MetS than the HSI, but additional research is needed to support this. Additionally, considering that the HSI has been

Table 2
Incidence and hazard ratios for incidence of metabolic syndrome according to non-alcoholic fatty liver disease indices.

	MetS incidence n (%)	Unadjusted HR (95 % CI)	Model 1 ^a (95 % CI)	Model 2 ^b (95 % CI)	Model 3 ^c (95 % CI)
Overall	2286 (43.6)				
Fatty liver index					
Per 1-SD increment		1.891 (1.810–1.976)	2.105 (2.008–2.206)	1.703 (1.586–1.829)	1.707 (1.590–1.834)
Cut-off value of score ^d					
< 30	1393 (35.9)	Reference	Reference	Reference	Reference
≥ 30 and <60	691 (63.3)	2.402 (2.192–2.633)	2.717 (2.470–2.988)	1.720 (1.534–1.929)	1.717 (1.531–1.926)
≥ 60	202 (73.5)	3.692 (3.183–4.283)	4.541 (3.892–5.298)	2.170 (1.798–2.618)	2.177 (1.803–2.627)
Hepatic steatosis index					
Per 1-SD increment		1.679 (1.610–1.751)	1.751 (1.680–1.825)	1.342 (1.238–1.455)	1.324 (1.220–1.436)
Cut-off value of score ^d					
< 30	448 (25.8)	Reference	Reference	Reference	Reference
≥ 30 and <36	1342 (48.3)	2.179 (1.958–2.426)	2.465 (2.210–2.749)	1.697 (1.485–1.939)	1.674 (1.465–1.913)
≥ 36	496 (68.2)	4.104 (3.610–4.666)	4.780 (4.192–5.450)	2.085 (1.700–2.556)	2.078 (1.694–2.548)

HR, hazard ratio; CI, confidence interval; SD, standard deviation; MetS, metabolic syndrome; MET, metabolic equivalent.

^a Model 1: Adjustment for age (per 1-year) and sex.

^b Model 2: Adjustment for age, sex, body mass index, smoking status, alcohol consumption, physical activity (per 1 METs-hour/week), income level, and education.

^c Model 3: Adjustment for age, sex, body mass index, smoking status, alcohol consumption, physical activity (per 1 METs-hour/week), income level, education, hypertension, diabetes mellitus, and dyslipidemia.

^d The cut-off value of the score refers to the value used to diagnose NAFLD for each index.

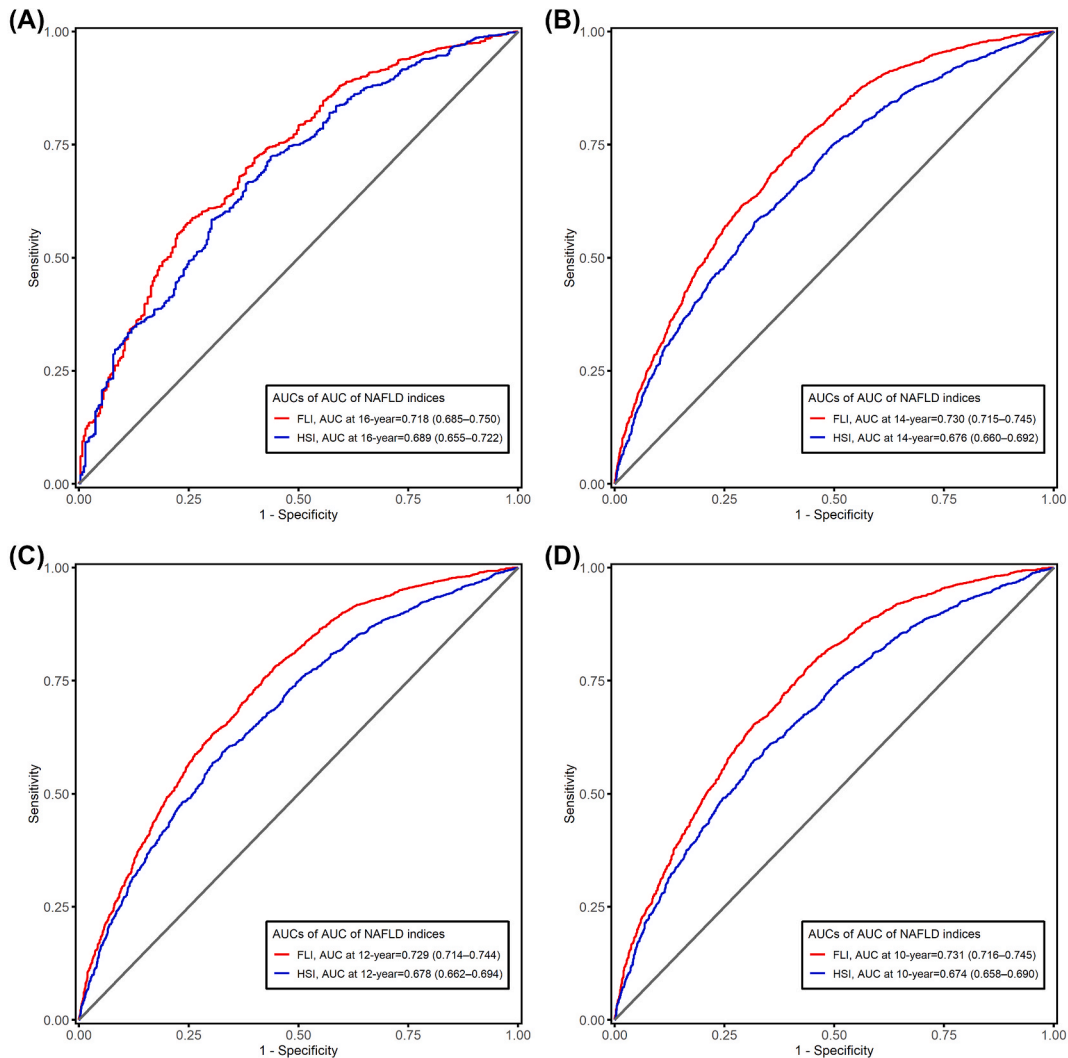


Fig. 3. Time-dependent ROC curves for predictive ability of NAFLD indices for MetS incidence during the follow-up period. MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; ROC, receiver operating characteristic.

Table 3
Comparison of predictive ability for incident metabolic syndrome between fatty liver index and hepatic steatosis index.

	Fatty liver index	Hepatic steatosis index	p-value
AUC from time-dependent ROC curve			
16-year	0.718 (0.685–0.750)	0.689 (0.655–0.722)	0.052 ^a
14-year	0.730 (0.715–0.745)	0.676 (0.660–0.692)	<0.001 ^a
12-year	0.729 (0.714–0.744)	0.678 (0.662–0.694)	<0.001 ^a
10-year	0.731 (0.716–0.745)	0.674 (0.658–0.690)	<0.001 ^a
Harrell's C-index	0.687 (0.676–0.697)	0.649 (0.637–0.660)	<0.001 ^a
^b IDI	0.027 (0.012–0.041)	Reference	0.027
^b NRI	0.047 (–0.003–0.093)	Reference	0.08

AUC, area under the receiver operating characteristic curve; ROC, receiver operating characteristic; IDI, integrated discrimination improvement; NRI, net reclassification improvement.

^a p-value for comparing the AUC from the time-dependent ROC curve and Harrell's C-index of the fatty liver index and hepatic steatosis index in predicting the incidence of metabolic syndrome.

^b IDI and NRI demonstrate the reclassification improvement when using the fatty liver index compared with the hepatic steatosis index in predicting the incidence of metabolic syndrome.

developed and validated in Koreans, these results may be even more interesting [14].

The findings of the present study have several important clinical implications. In large-scale studies or health checkups, methods such as the FLI and HSI, which are simpler and easier to apply than accurate diagnostic methods such as liver biopsies for NAFLD, may be more clinically useful. Because MetS is associated with an increased risk of cardiovascular diseases, type 2 diabetes, and overall mortality, early detection and prevention at the population level are crucial. Implementing the FLI and HSI in routine screenings can enhance the early identification of individuals at risk for MetS as well as NAFLD, providing a practical and non-invasive approach to risk assessment. These indices, derived from commonly measured clinical parameters, facilitate the timely detection of metabolic dysfunction, enabling earlier interventions and potentially reducing the overall burden of cardiometabolic diseases through preventive strategies.

This study used a large sample size and long-term follow-up data from a cohort with comprehensive information. However, this study had some limitations. First, the study population was restricted to middle-aged Korean adults, which may limit the generalizability of the results to other ethnicities or age groups. Second, the observational nature of this study precludes causal inferences. Furthermore, we did not account for sequential changes in the FLI and HSI over time, considering only the baseline measurements. This could have impacted the assessment of their predictive power for incident MetS. Studies investigating the impact of sequential changes in the FLI and HSI on MetS risk can offer deeper insights into their utility as dynamic markers of metabolic health. Finally, we lacked data on certain medications and other potential confounders that might have influenced MetS incidence. Despite these limitations, our findings provide valuable insights into preventive public health strategies for populations at high risk of developing MetS. Future studies should consider longitudinal analyses that account for changes in NAFLD indices over time to provide a more dynamic understanding of their predictive power.

In conclusion, this study suggests that the FLI and HSI are closely associated with MetS in middle-aged Korean adults. Specifically, both indices are valuable not only for identifying individuals who currently have metabolic syndrome but also for predicting those at risk of developing it in the future. The FLI, in particular, showed superior predictive power in both contexts, highlighting its utility in clinical and public health settings for comprehensive metabolic health assessment. Given the increasing prevalence of MetS and its health implications, incorporating the FLI into clinical practice can improve early detection and intervention strategies. Future research should investigate the applicability of the FLI in diverse populations and its role in comprehensive MetS management protocols.

CRediT authorship contribution statement

Byung Sik Kim: Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Hyun-Jin Kim:** Writing – review & editing, Writing – original draft, Conceptualization. **Seong Won Jeon:** Writing – review & editing, Conceptualization. **Kyung Hwan Kim:** Writing – review & editing, Data curation, Conceptualization. **Dong Wook Kim:** Writing – review & editing, Formal analysis, Conceptualization. **Jeong-Hun Shin:** Writing – review & editing, Supervision, Conceptualization.

Data availability statement

This study used data from the Ansan–Ansung cohort, which is part of the Korean Genome and Epidemiology Study. The dataset is publicly available through the Korean National Institute of Health at the following website: <https://coda.nih.go.kr/usab/koges/intro.do> (accessed December 2023).

Ethics declaration

This study was reviewed and approved by the Korean National Institute of Health and the Institutional Review Board of Hanyang University Guri Hospital (approval no. GURI-2023-06-020), dated June 2023. All participants provided written informed consent to participate in the study and for their data to be published. The study protocol adhered to the principles of the Declaration of Helsinki.

Funding

This work was supported by a research fund from Hanyang University (HY202400000001252). The funders had no role in the design of the study; the collection, analysis, or interpretation of data; the writing of the manuscript; or the decision to publish the results.

Declaration of competing interest

None.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2025.e43073>.

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