

Clínica Universidad de Navarra-Body Adiposity Estimator Index as A Predictor of Metabolic Dysfunction-associated Steatotic Liver Disease: A Large-scale Cross-sectional Analysis

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Received: 05.03.2025

Accepted: 17.07.2025

ABSTRACT

Background & Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) affects 32.4% of the global population and is a major cause of chronic liver disease and cardiometabolic complications. Early detection is challenging due to limitations of conventional obesity indices like body mass index (BMI) and waist circumference (WC), which do not account for age- and sex-specific adiposity variations. The Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) index, integrating BMI, age, and gender, may offer a better measure of body fat percentage, but its utility in MASLD prediction is unexplored. We aimed to evaluate the predictive value of the CUN-BAE index for MASLD and to compare it with conventional obesity indices.

Methods: 1,003 participants from Guang'anmen Hospital were recruited (2023–2024). MASLD diagnosis was based on established criteria, and participants underwent clinical and laboratory assessments. Logistic regression models were used to determine the association between the CUN-BAE index and MASLD, with predictive performance assessed using area under the receiver operating characteristic curve (AUROC).

Results: Among 949 participants, 555 (58.5%) had MASLD. The CUN-BAE index showed a significant positive association with MASLD risk (Model 3: OR=1.16, 95%CI: 1.12-1.20, $p<0.001$). Its AUROC (0.677) surpassed BMI (0.612) and WC (0.598), especially in women (AUROC=0.809 vs. BMI=0.721, WC=0.698) compared to men (AUROC=0.664 vs. BMI=0.603, WC=0.591). A dose-response relationship was observed, with increased CUN-BAE levels correlating with higher MASLD risk beyond a threshold of 29.097.

Conclusions: The CUN-BAE index is a robust predictor of MASLD, outperforming BMI and WC, particularly in women. It captures age- and gender-specific adiposity variations, enhancing its utility as a non-invasive screening tool. Future research should focus on longitudinal validation and integrating additional metabolic parameters.

Key words: MASLD – CUN-BAE index – obesity indices – metabolic syndrome – body adiposity – predictive model.

Abbreviations: AUROC: area under the receiver operating characteristic curve; BMI: body mass index; CAP: controlled attenuation parameter; CI: confidence interval; CUN-BAE: The Clínica Universidad de Navarra-Body Adiposity Estimator; MASLD: metabolic dysfunction-associated steatotic liver disease; MRI-PDFF: magnetic resonance imaging proton density fat fraction; MetS: metabolic syndrome; OR: odds ratio; T2DM: type 2 diabetes mellitus; WC: waist circumference; WtHR: waist-to-height ratio.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become one of the most prevalent chronic liver disorders, affecting approximately 32.4% of the global adult population [1, 2]. It is a leading cause of cirrhosis,

hepatocellular carcinoma and increased cardiovascular risk [3, 4]. MASLD is closely associated with metabolic syndrome (MetS), obesity, insulin resistance and type 2 diabetes mellitus (T2DM), which have significantly contributed to its increasing global burden [5, 6]. Despite its rising prevalence, MASLD remains underdiagnosed in clinical practice, primarily due to the lack of cost-effective and widely applicable screening tools [7, 8]. Currently, liver biopsy is still considered the gold standard for diagnosing MASLD and assessing hepatic fibrosis. However, its invasive nature, high cost and potential

complications limit its feasibility for widespread screening [9, 10]. Imaging modalities, such as transient elastography, magnetic resonance imaging proton density fat fraction (MRI-PDFF) and controlled attenuation parameter (CAP), have emerged as non-invasive alternatives for evaluating liver fat content [11,12]. However, their high costs and limited accessibility present significant barriers to routine clinical implementation, particularly in resource-limited settings. Consequently, there is an urgent need for simple, non-invasive and cost-effective anthropometric indices to predict MASLD risk at the demographic level [13].

Obesity and lipid metabolism disorders are important causes of MASLD. In clinical practice, body mass index (BMI) and waist circumference (WC) are commonly used as indicators of obesity and metabolic risk. However, these measures do not differentiate between fat mass and lean mass, limiting their ability to predict metabolic abnormalities [14, 15]. This is particularly evident in conditions such as lean MASLD, where individuals develop hepatic steatosis despite having a normal BMI [16]. Studies have demonstrated that BMI alone fails to capture visceral adiposity, which plays a crucial role in the pathogenesis of MASLD and insulin resistance [17, 18]. Therefore, alternative obesity indices that better reflect body fat distribution are needed to improve MASLD risk assessment.

The Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) index is an emerging anthropometric index designed to estimate body fat percentage based on BMI, age and gender [19]. Unlike BMI, which only accounts for total body mass, CUN-BAE incorporates age- and gender-specific variations in adiposity, making it a more precise indicator of metabolic health [20]. Recent studies have demonstrated that CUN-BAE outperforms traditional obesity indices in predicting metabolic diseases [21, 22]. The CUN-BAE index may provide a more nuanced assessment of metabolic risk compared with BMI or WC. In addition, studies have shown that the CUN-BAE index is closely related to cardiovascular events, subclinical atheromatosis, MetS, body fat abnormalities and other metabolic diseases [23-26].

The authors hypothesise that the CUN-BAE index, which accounts for age- and gender-specific adiposity, may reliably predict MASLD risk. This study aims to evaluate the association between the CUN-BAE index and MASLD using a large-scale cross-sectional dataset and to examine sex-specific differences in its diagnostic performance. The findings may establish practical CUN-BAE cut-off values for MASLD screening, improving early detection and risk stratification in clinical practice.

METHODS

Participants

A total of 1,003 volunteers were recruited for this study between January 2023 and November 2024 at Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval no. 2023-155-KY-01). The study protocol was reviewed and approved by the Hospital Ethics Committee in accordance with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants

before their inclusion in the study. The diagnostic criteria for MASLD were based on the recommendations outlined in The Guidelines for the Prevention and Treatment of Metabolic Dysfunction-Associated (Non-Alcoholic) Fatty Liver Disease (Version 2024) [27]. The detailed diagnostic criteria are as follows:

1. Confirmation of fatty liver
 - Imaging evidence: confirmed by imaging studies, such as ultrasound, CAP or MRI-PDFF ($\geq 5\%$).
 - Histological evidence from liver biopsy: hepatocellular macrovesicular steatosis $\geq 5\%$.
2. Presence of metabolic dysfunction
 - Patients must meet at least one of the following components of MetS:
 - Overweight/obesity: BMI ≥ 24.0 kg/m² or WC ≥ 90 cm (men)/85 cm (women).
 - Abnormal glucose metabolism: Prediabetes (fasting blood glucose ≥ 6.1 mmol/L or HbA1c $\geq 5.7\%$) or diagnosed T2DM.
 - Dyslipidaemia: Fasting triglycerides (TGs) ≥ 1.70 mmol/L or reduced high-density lipoprotein cholesterol (HDL-C) (men < 1.0 mmol/L, women < 1.3 mmol/L).
 - Hypertension: Blood pressure $\geq 130/85$ mmHg or on antihypertensive treatment.
3. Exclusion of other causes
 - Excessive alcohol consumption [27]: men < 210 g of ethanol per week, women < 140 g per week
 - Other secondary causes of fatty liver [27]: for example, drug-induced liver injury, viral hepatitis (excluding genotype 3 hepatitis C virus infection), Wilson's disease or malnutrition. Active infections were ruled out via serological testing (positive HBsAg or anti-HCV).

Special situations:

- Mixed fatty liver disease: if a patient has concurrent alcoholic liver disease (ALD) or other causes of fatty liver but also has obesity, type 2 diabetes mellitus or components of MetS, they should be diagnosed with MASLD combined with ALD or other liver diseases (e.g. 'MASLD+ALD').
- Concurrent chronic viral hepatitis: MASLD can coexist with conditions such as chronic hepatitis B and chronic hepatitis C. Each condition should be diagnosed separately, and the impact of metabolic factors on disease progression should be assessed.
- Preferential use of non-invasive assessment: Ultrasound is the first-line screening method. Controlled attenuation parameter/liver stiffness measurement and MRI-PDFF are used for assessing fat content and fibrosis. Liver biopsy is reserved for uncertain cases or clinical research.

To rigorously evaluate the pathophysiology specific to MASLD, patients meeting any of these 'special situation' criteria (including MASLD+ALD, MASLD with viral hepatitis, or other multifactorial etiologies) were systematically excluded from the analytic cohort. This ensures our study focuses exclusively on *pure* MASLD cases without confounding comorbidities.

The inclusion criteria of this study were as follows: (1) participants aged 18–75 years; (2) availability of complete liver images and laboratory test results; and (3) provision

of signed informed consent. The exclusion criteria were as follows: (1) pregnant or lactating women; (2) individuals with severe diseases affecting the brain, heart, lungs, kidneys or blood system, as well as those with mental health disorders (excluding hypertension, diabetes mellitus and hyperlipidaemia requiring medication); (3) individuals diagnosed with drug-induced hepatitis, autoimmune liver disease or hepatocellular carcinoma. Participants without a diagnosis of MASLD, a history of liver disease or abnormal liver function were classified as the healthy control group. A total of 54 volunteers were excluded due to missing imaging data (n=30) or pregnancy/lactation (n=24).

Collection of clinical data

Participants underwent an overnight fasting period of ≥ 8 hours, after which fasting blood samples were collected in the early morning of the following day. These samples were analysed in the hospital's laboratory for various parameters, including blood count, liver function, kidney function, lipid profile and glycated haemoglobin levels.

Definitions

The CUN-BAE index was calculated using the following formula:

$$\text{CUN-BAE} = -44.988 + (3.172 \times \text{BMI}) + (10.689 \times \text{gender}) + (0.503 \times \text{age}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{gender}) - (0.02 \times \text{BMI} \times \text{age}) + (0.00021 \times \text{BMI}^2 \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{gender}).$$

Male = 0; Female = 1.

Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, a previous diagnosis of hypertension or current use of antihypertensive drugs. Type 2 diabetes mellitus was defined as (FBG ≥ 7.0 mmol/L or HbA1c $\geq 6.5\%$) or previous diagnosis of T2DM or current use of glucose-lowering drugs.

Data analysis

Statistical analysis was performed following the guidelines provided by the Centers for Disease Control and Prevention (<https://www.cdc.gov/nchs/nhanes/tutorials/default.aspx>) using R software (<http://www.R-project.org>, The R Foundation, version 3.4.3). Data with a normal distribution were presented as mean \pm standard deviation, and non-normally distributed data were reported as median and interquartile range (25%, 75%). Comparisons between the MASLD and non-MASLD groups were conducted using appropriate statistical tests: Student's *t*-test for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed continuous variables and the chi-squared test for categorical variables. Three logistic models were developed to explore the association between the CUN-BAE index and MASLD risk. Model 1 contained only independent variables; Model 2 was adjusted for gender and age; Model 3 was further adjusted for BMI. Results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Before performing logistic regression, the covariance of the different models was

tested. Restricted cubic spline curves were used to analyse the dose-response relationship between the CUN-BAE index and the risk of MASLD. The area under the receiver operating characteristic curve (AUROC), sensitivity and specificity were used to evaluate the predictive effect of the CUN-BAE indexes on MASLD. All tests were considered statistically significant at $p < 0.05$.

RESULTS

Characteristics of the Participants

Among the 949 participants, 555 had MASLD. The proportion of men and women was 60.70% and 39.30%, respectively. The median age was 47 (37, 58) years. Participants with and without MASLD had statistically different baseline characteristics, except for gender. Participants with MASLD were more likely to be older and have hypertension, diabetes and high cholesterol. More importantly, participants with MASLD had higher BMI, SBP, DBP, aspartate aminotransferase, alanine transaminase, gamma-glutamyl transferase, low-density lipoprotein cholesterol and CUN-BAE levels, as well as higher TG levels and lower HDL-C levels compared with the non-MASLD group (Table I).

The Associations between the CUN-BAE Index and MASLD

Table II shows the multivariate-adjusted ORs and 95% CIs of MASLD risks in relation to CUN-BAE index levels. In the unadjusted model (Model 1), each quartile increment in the CUN-BAE index was associated with a 10% increase in MASLD risk (OR=1.10, 95%CI: 1.08–1.12, $p < 0.001$). After adjusting for sex and age (Model 2), the association remained significant (OR=1.35, 95%CI: 1.01–1.79, $p = 0.038$). Further adjustment for BMI (Model 3) showed that the CUN-BAE index was positively correlated with the risk of MASLD (OR=1.16, 95%CI: 1.12–1.20, $p < 0.001$).

Dose-response Relationships between the CUN-BAE Index and MASLD

Dose-response curves for the relationships between the CUN-BAE index and the risk of MASLD are presented in Fig. 1. There was a positive non-linear correlation between MASLD and the CUN-BAE index (p overall < 0.001 , p non-linear < 0.011). When the CUN-BAE level was low, it was protective against MASLD; however, its protective effect gradually diminished as the CUN-BAE level increased. A nonlinear dose-response relationship was observed, with significantly elevated MASLD risk emerging above the CUN-BAE threshold of 29.097. When the CUN-BAE index exceeded a certain threshold (29.097), the risk of MASLD prevalence increased continuously with increasing CUN-BAE levels.

Use of the CUN-BAE Index to Predict MASLD

Table III and Figures 2–4 show the AUROC values (95% CI) of the CUN-BAE index for screening adults with MASLD. Overall, the AUROC of the CUN-BAE index in predicting MASLD was 0.677 (0.646, 0.707), with a cut-off of 31.69, a sensitivity of 78.93 and a specificity of 47.57%.

Table I. Basic characteristics of participants by MASLD

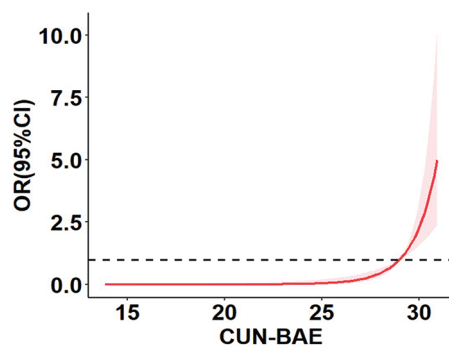
Characteristic	Overall (n = 949)	Non-MASLD (n= 394)	MASLD (n= 555)	p
Age (years)	47 (37, 58)	40 (35, 48)	52 (43, 62)	<0.001
Male, n (%)	576 (60.70)	253 (64.21)	323 (58.20)	
BMI (kg/m ²)	25.6 (23.2, 27.8)	24.4 (22.1, 26.5)	26.2 (24.2, 28.4)	<0.001
SBP (mmHg)	130 (120, 141)	125 (116, 135)	134 (122, 145)	<0.001
DBP (mmHg)	79 (72, 88)	77 (70, 85)	81 (74, 90)	<0.001
ALT (IU/L)	27 (20, 37)	21 (14, 30)	30 (24, 41)	<0.001
AST (IU/L)	23 (19, 28)	19 (16, 23)	25 (22, 30)	<0.001
GGT (IU/L)	23 (16, 34)	20 (14, 29)	25 (17, 37)	<0.001
TG (mmol/L)	1.31 (0.91, 1.81)	1.06 (0.73, 1.46)	1.47 (1.11, 2.00)	<0.001
HDL-C (mmol/L)	1.21 (1.04, 1.40)	1.33 (1.15, 1.51)	1.12 (1.00, 1.30)	<0.001
LDL-C (mmol/L)	2.67 (2.16, 3.23)	2.59 (2.16, 3.08)	2.73 (2.16, 3.35)	0.010
CUN-BAE Index	29 (24, 35)	27 (23, 31)	31 (26, 38)	<0.001
Hypertension, n (%)	373 (39.30)	33 (8.38)	340 (61.26)	<0.001
T2DM	183 (19.28)	20 (5.08)	163 (29.37)	<0.001
High Cholesterol	443 (46.68)	29 (7.36)	414 (74.59)	<0.001

MASLD: metabolic dysfunction-associated steatotic liver disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CUN-BAE: Clínica Universidad de Navarra-Body Adiposity Estimator; T2DM: type 2 diabetes mellitus.

Table II. Multi-variate adjusted ORs (95% CIs) of MASLD in relation to quartile increment of CUN-BAE index

Variables	Model 1	p	Model 2	p	Model 3	p
CUN-BAE	1.10	<0.001	1.35	0.038	1.16	<0.001
	[1.08, 1.12]		[1.01, 1.79]		[1.12, 1.20]	

Model 1 contained only independent variables. Model 2 was adjusted for sex and age. Model 3 was further adjusted for BMI; OR: Odds Ratio; CI: Confidence Interval. For the rest of abbreviations see Table I.

**Fig. 1.** Dose-response relationships between Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) levels and the risk of Metabolic dysfunction-associated steatotic liver disease (MASLD) with restricted cubic spline model.

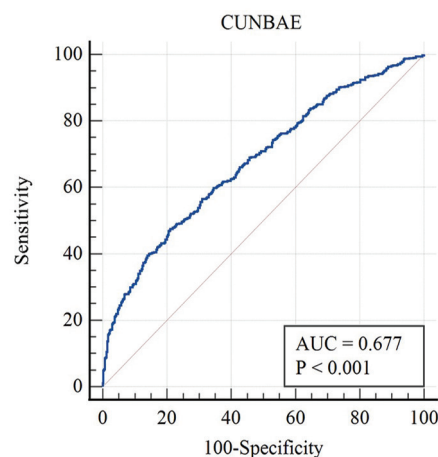
For men, the AUROC of the CUN-BAE index in predicting MASLD was 0.664 (0.624, 0.703), with a cut-off of 23.39, a sensitivity of 78.95 and a specificity of 46.25%.

For women, the AUROC of the CUN-BAE index in predicting MASLD was 0.809 (0.765, 0.847), with a cut-off of 34.21, a sensitivity of 85.78 and a specificity of 62.41%.

Table III. CUN-BAE for predicting MASLD and the corresponding AUC, optimal cut-off values, their sensitivity and specificity, PPV and NPV

Variable	AUC (95%CI)	Cut-off Values	Sensitivity (%)	Specificity (%)	p
Overall	0.677 (0.646, 0.707)	31.69	78.93	47.57	<0.001
Male	0.664 (0.624, 0.703)	23.39	78.95	46.25	<0.001
Female	0.809 (0.765, 0.847)	34.21	85.78	62.41	<0.001

AUC: Area Under the Curve. For the rest of abbreviations see Table I and II.

**Fig. 2.** Receiver operating characteristic curves of Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) in overall for identifying Metabolic dysfunction-associated steatotic liver disease (MASLD).

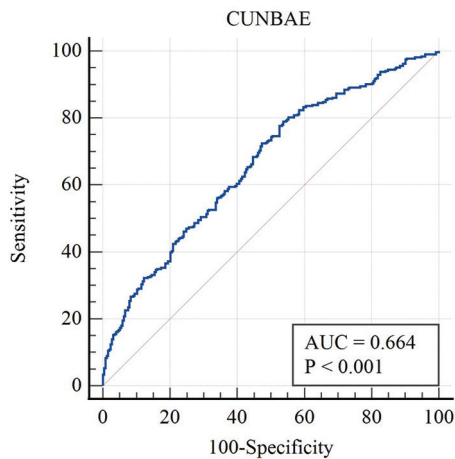


Fig. 3. Receiver operating characteristic curves of Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) in male for identifying Metabolic dysfunction-associated steatotic liver disease (MASLD).

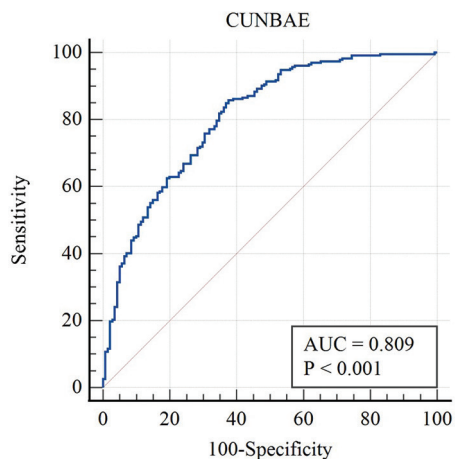


Fig. 4. Receiver operating characteristic curves of Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) in female for identifying Metabolic dysfunction-associated steatotic liver disease (MASLD).

DISCUSSION

Metabolic associated steatotic liver disease has become a global health challenge, with its prevalence rising in parallel with the obesity epidemic and MetS. Early identification of individuals at risk for MASLD is critical for effective prevention and intervention. Although traditional anthropometric indices, such as BMI and WC, have been widely used to assess obesity-related metabolic risks, their inability to account for age- and sex-specific variations in adiposity limits their predictive accuracy. The CUN-BAE index, which incorporates BMI, age and gender, has emerged as a promising tool for estimating body fat percentage and predicting metabolic risks. In this large-scale cross-sectional study, we evaluated the association between the CUN-BAE index and MASLD risk, demonstrating that the CUN-BAE index is significantly associated with MASLD, particularly in women. Our findings suggest that the CUN-BAE index outperforms traditional obesity indices in predicting

MASLD risk, offering a more nuanced approach to adiposity assessment.

This large-scale cross-sectional study provides evidence that the CUN-BAE index, a validated measure of body adiposity, is significantly associated with the risk of MASLD. Our findings are in line with previous research suggesting that adiposity indices, such as CUN-BAE, BMI and WC, are robust predictors of MASLD [28-30]. However, the CUN-BAE index offers a more nuanced approach by incorporating age, gender and BMI, which may explain its superior predictive accuracy in certain subgroups, particularly among women. Our study results are consistent with the recent large-scale study by Wang et al. [31], which validated the robustness of the CUN-BAE index as a predictive tool for MASLD in a Japanese population. Both studies reported stronger associations and diagnostic accuracy in women, reinforcing the gender-specific value of the index. However, the differences in AUROC values (0.809 in women vs 0.893) and cut-off values (29.1 vs 33.25) may reflect population heterogeneity, differences in inclusion criteria and methodological variations. For example, the exclusion of diabetic patients in Wang's study may have increased specificity, while our broader inclusion criteria covered a higher-risk population. These comparisons highlight the importance of tailoring CUN-BAE cut-off values according to local population characteristics and clinical contexts. Future research should prioritise multi-ethnic validation to establish universal standards.

The CUN-BAE index has been widely validated as a reliable measure of body fat percentage, particularly in populations with varying degrees of adiposity [32]. Recent studies have demonstrated that the CUN-BAE index outperforms traditional obesity indices in predicting metabolic diseases. For instance, Peng et al. [21] found that each 1-unit increase in the CUN-BAE index was associated with a 1.08-fold and 1.14-fold increased risk of diabetes in men and women, respectively. Similarly, Dominguez et al. [22] reported that a 2-unit increase in CUN-BAE was linked to a 27% and 29% higher risk of hypertension in men and women, respectively. These findings suggest that the CUN-BAE index may provide a more nuanced assessment of metabolic risk compared with BMI or WC, particularly in capturing age- and sex-specific variations in adiposity. In addition, studies have shown that the CUN-BAE index is closely related to cardiovascular events, subclinical atheromatosis, MetS, body fat abnormalities and other metabolic diseases [23-26]. In our study, the CUN-BAE index demonstrated a strong positive correlation with MASLD risk, even after adjusting for confounding factors, including but not limited to age, gender, and BMI. This finding is consistent with recent studies highlighting the role of visceral adiposity in the pathogenesis of MASLD [33, 34]. However, the CUN-BAE index is not without limitations. Since BMI does not distinguish between fat mass and lean mass, its use as a primary input may introduce bias [35]. Future iterations of the CUN-BAE index could be improved by integrating additional anthropometric measures, such as waist-to-hip ratio or bioelectrical impedance analysis, to improve its accuracy [36, 37].

One of the most intriguing findings of our study is the greater predictive performance of the CUN-BAE index in women compared with men. The AUROC for women was

0.809, significantly higher than the 0.664 observed in men. This discrepancy may be attributed to differences in fat distribution and hormonal influences between gender. Women tend to have a higher proportion of subcutaneous fat, which is metabolically less active than visceral fat but may still play a role in MASLD risk dysregulation [38, 39]. Additionally, oestrogen has been shown to exert protective effects against hepatic steatosis, which may explain the lower prevalence of MASLD in premenopausal women [40]. Although the waist-to-height ratio (WtHR) has shown slightly higher AUROC values in some studies [41], the CUN-BAE index, by incorporating age and gender, provides a more comprehensive and nuanced assessment of metabolic risk. This makes the CUN-BAE index particularly useful for identifying individuals at risk of MASLD, especially in populations with significant age and gender differences, such as women. We believe that the CUN-BAE index is a valuable addition to the non-invasive toolset for MASLD risk assessment, offering a more detailed and personalised approach to identifying at-risk populations.

In our clinical practice, we have observed that postmenopausal women often exhibit a marked increase in visceral fat accumulation and MASLD incidence, suggesting that hormonal changes play a critical role in disease progression. This is supported by recent studies showing that oestrogen replacement therapy in postmenopausal women can reduce liver fat content and improve insulin sensitivity [42]. However, the protective effects of oestrogen may be counteracted by factors such as increased adiposity and reduced physical activity, both prevalent in this demographic. These observations highlight the need for targeted interventions, such as hormone therapy or lifestyle modifications, in postmenopausal women at risk for MASLD.

The CUN-BAE index shows promise as a tool for MASLD risk stratification in clinical practice. Its simplicity and ease of calculation make it an attractive alternative to invasive methods, such as liver biopsy, or imaging-based techniques for fat quantification [43, 44]. In clinical settings, the CUN-BAE index could be integrated into routine health check-ups as a first-line screening tool for MASLD, particularly in resource-limited settings where advanced diagnostic tools are unavailable. For individuals with elevated CUN-BAE values, further evaluation using imaging techniques (e.g. transient elastography or MRI-PDFF) or metabolic biomarkers (e.g. adiponectin or leptin) could be considered to confirm the diagnosis and assess disease severity [45, 46]. Additionally, lifestyle interventions, such as dietary modifications and physical activity programmes, could be tailored based on CUN-BAE values to reduce MASLD risk, particularly in high-risk populations, such as postmenopausal women [47, 48]. However, its application in men may require a combination with other indicators to improve predictive accuracy. Future studies should further validate the applicability of the CUN-BAE index in different populations and explore its optimal use in clinical practice.

Our study also highlights the need for a deeper exploration of the complex interplay between adiposity and MASLD. Although the CUN-BAE index provides valuable insights, it is important to recognise that adiposity is only one component of a complex MetS. Recent studies indicate that gut microbiota

composition, systemic inflammation and mitochondrial dysfunction are integral to MASLD pathogenesis [49, 50]. Future research should aim to integrate these factors into predictive models to provide a broader, more precise risk assessment for MASLD.

Despite its strengths, our study has several limitations. Firstly, the cross-sectional design precludes the establishment of causal relationships between the CUN-BAE index and MASLD risk. Longitudinal studies are needed to determine whether changes in the CUN-BAE index over time correlate with MASLD progression or regression. Secondly, our study population was predominantly composed of East Asian individuals recruited from a single centre, which may limit the generalisability of our findings to other ethnic groups or regions. Future studies should include diverse populations to validate the CUN-BAE index across different genetic and environmental backgrounds. Thirdly, the CUN-BAE index relies on BMI as a primary input, which does not distinguish between fat mass and lean mass. This limitation may introduce bias, particularly in individuals with high muscle mass or sarcopenia. Future iterations of the CUN-BAE index could be improved by integrating additional anthropometric measures, such as waist-to-hip ratio or bioelectrical impedance analysis, to enhance its accuracy. In addition, in this study, we employed multiple methods to diagnose hepatic steatosis, including ultrasound, CAP from transient elastography and MRI-PDFF. Each of these methods has its own strengths and limitations, which may have certain impacts on the study results. Ultrasound is a non-invasive, low-cost and widely used imaging method that can provide an initial assessment of hepatic steatosis. However, its accuracy relies on the operator's experience and subjective judgment, which may lead to inconsistencies in diagnostic results. Moreover, ultrasound has lower sensitivity for mild steatosis and may miss some early cases. Controlled attenuation parameter is a non-invasive and quantitative assessment method that provides a numerical evaluation of liver fat content. However, the accuracy of CAP may be affected by liver inflammation and fibrosis, leading to false-positive or false-negative results. Additionally, the availability of CAP devices and the technical requirements for operation may limit its application in some clinical settings. Magnetic resonance imaging proton density fat fraction is a high-precision non-invasive assessment method that provides accurate measurement of liver fat content. However, MRI-PDFF is costly and has high requirements for equipment and technical expertise, which may limit its widespread use in routine clinical practice. Moreover, the longer examination time of MRI-PDFF may affect patient acceptance. These limitations of diagnostic methods may have certain impacts on the study results. For example, ultrasound may miss mild steatosis, whereas MRI-PDFF may provide a more accurate assessment. This may affect the strength of the association between the CUN-BAE index and MASLD risk. In clinical practice, the choice of appropriate diagnostic methods needs to take into account cost, availability and accuracy. Although MRI-PDFF provides the most accurate assessment, its high cost and limited accessibility may restrict its use in large-scale screening. We acknowledge potential overadjustment in Model 3 due to BMI's integral role in the CUN-BAE

formula. The resulting mathematical coupling may attenuate effect estimates, rendering the residual CUN-BAE-MASLD association a conservative estimate. Future studies should utilize BMI-independent adiposity measures (e.g., waist-hip ratio, DEXA) to validate these findings. Therefore, ultrasound and CAP may be more suitable as initial screening tools in resource-limited settings.

CONCLUSIONS

The CUN-BAE index demonstrates enhanced MASLD prediction in women by integrating BMI, age and gender-specific metabolic changes. While clinically promising for female risk stratification, its moderate performance in men (with lower AUROC than WtHR) necessitates complementary approaches for male populations. Future validation in diverse cohorts should confirm cross-demographic applicability, and longitudinal studies must define its role in tracking MASLD progression. When used judiciously - particularly as a preliminary screening tool for women - this index advances precision adiposity assessment.

Conflicts of interest: None to declare.

Authors' contributions: Z.Z. conceived and designed the study. H.P., X.Y., Z.G and J. W collected the data. All the authors analyzed and interpreted the data. Z.Z and W.L. performed the statistical analysis. Z.Z. supervised the project and drafted the manuscript. All the authors critically revised the paper and approved the final version of the manuscript.

Acknowledgements: Special Project on Evidence-Based Research in Traditional Chinese Medicine - High Level Chinese Medical Hospital Promotion Project (No. HLCMHPP2023086).

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