Establishment and evaluation of a noninvasive metabolism-related fatty liver screening and dynamic monitoring model: cross-sectional study

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Jiali Ni[1*]; Yong Huang[2*]; Qiangqiang Xiang[1*]; Qi Zheng[1]; Xiang Xu[2]; Zhiwen Qin[2]; Guoping Sheng[2] MD; Lanjuan Li[3] MD

[1]The First Affiliated Hospital, School of Medicine, Zhejiang University Hangzhou CN
[2]Shulan (Hangzhou) Hospital Affiliated to Zhejiang Shuren University, Shulan International Medical College Hangzhou CN
[3]State Key Laboratory for Diagnosis and Treatment of Infectious Disease, the First Affiliated of Hospital Hangzhou CN
[*]these authors contributed equally

Corresponding Author:
Lanjuan Li MD
State Key Laboratory for Diagnosis and Treatment of Infectious Disease, the First Affiliated of Hospital
Zhejiang University School of Medicine, Hangzhou, 310003
Hangzhou
CN

Abstract

Background: Metabolically associated fatty liver disease (MAFLD) insidiously affects people's health, and many models have been proposed for the evaluation of liver fibrosis. However, there is still a lack of no-invasive and sensitive models for screening MAFLD in high-risk populations.

Objective: The purpose of this study was to explore a new method for early screening in public, and established a tool for regular self-assessment of MAFLD.

Methods: Two thousand participants were enrolled in this cross-sectional study. Routine blood, blood biochemistry and FibroScan tests were performed, and body composition was analysed by a body composition instrument. Additionally, multiple factors were also recorded, including disease-related risk factors, the Forns index score, the hepatic steatosis index (HSI) score, the triglyceride glucose index (TyG) score, total body water (TBW), body fat mass (BFM), visceral fat area (VFA), the waist-to-height ratio (WHtR), and the basal metabolic rate (BMR). The new model, named the MAFLD Screening Index (MFSI), was established by binary logistic regression, and body fat mass, the waist-height ratio and total body water were included. A simple rating table, named the MAFLD Rating Table (MRT), was also established by the above indicators.

Results: The performance of the HSI (area under the curve (AUC): 0.873, specificity 76.8%, sensitivity 81.4%), the WHtR (AUC: 0.866, specificity 79.8%, sensitivity 80.8%), and BFM (AUC: 0.842, specificity 76.9%, sensitivity 76.2%) in discriminating between the MAFLD group and non-fatty liver group was evaluated (P<0.01). The AUC of the combined model including WHtR/HSI/BFM values was 0.900 (specificity: 81.8%, sensitivity: 85.6%, P<0.01). The MFSI was established based on better performance in screening MAFLD patients in the training set (AUC: 0.896, specificity 83.8%, sensitivity 82.1%) and was confirmed in the testing set (AUC: 0.917, specificity 89.8%, sensitivity 84.4%) (P<0.01).

Conclusions: The new MFSI model had better performance than the other models for early MAFLD screening. The new model showed strong power and stability and shows promise in the area of MAFLD detection and self-assessment. The MRT was practical to assess disease alterations in real time. Clinical Trial: cMetabolic-associated fatty liver disease; Nonalcoholic fatty liver disease; Nonalcoholic steatohepatitis; Body fat mass; Waist-to-height ratio; Basal metabolic rate.

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a: State Key Laboratory for Diagnosis, National Clinical Research Center for Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

b: Collaborative Innocation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, China

c: Department of Infectious Disease, Shulan (Hangzhou) Hospital Affiliated to Zhejiang Shuren University, Shulan International Medical College, Hangzhou 310022, China.

1: These authors contributed equally to this work.

Corresponding author: Guoping Sheng (gpsheng@zju.edu.cn); Lanjuan Li (M.D. Tel: 86-571-87236458; Fax: 86-571-87236459; ljli@zju.edu.cn)

Abstract

Background: Metabolically associated fatty liver disease (MAFLD) insidiously affects people's health, and many models have been proposed for the evaluation of liver fibrosis. However, there is still a lack of no-invasive and sensitive models for screening MAFLD in high-risk populations.

Objective: The purpose of this study was to explore a new method for early screening in public, and established a home-based tool for regular self-assessment and monitoring of MAFLD.

Methods: In this cross-sectional study, there were 1758 eligible participants in the training set and 200 eligible participants in the testing set. Routine blood, blood biochemistry and FibroScan tests were performed, and body composition was analysed by a body composition instrument. Additionally, multiple factors were also recorded, including disease-related risk factors, the Forns index score, the hepatic steatosis index (HSI) score, the triglyceride glucose index (TyG) score, total body water (TBW), body fat mass (BFM), visceral fat area (VFA), the waist-to-height ratio (WHtR), and the basal metabolic rate (BMR). Binary logistic regression was performed to explore the potential anthropometric indicators with well predictive ability for screening MAFLD. The new model, named the MAFLD Screening Index (MFSI), was established by binary logistic regression, and body fat mass, the waist-height ratio and total body water were included. A simple rating table, named the MAFLD Rating Table (MRT), was also established by the above indicators.

Results: The performance of the HSI (area under the curve (AUC): 0.873, specificity 76.8%, sensitivity 81.4%), the WHtR (AUC: 0.866, specificity 79.8%, sensitivity 80.8%), and BFM (AUC: 0.842, specificity 76.9%, sensitivity 76.2%) in discriminating between the MAFLD group and non-fatty liver group was evaluated (*P*<.001). The AUC of the combined model including WHtR/HSI/BFM values was 0.900 (specificity: 81.8%, sensitivity: 85.6%, *P*<.001). The MFSI was established based on better performance in screening MAFLD patients in the training set (AUC: 0.896, specificity 83.8%, sensitivity 82.1%) and was confirmed in the testing set (AUC: 0.917, specificity 89.8%, sensitivity 84.4%) (*P*<.001).

Conclusion: The novel model MFSI built by WHtR, BFM, and TBW for the screening of early MAFLD. The body parameters can be easily obtained by body fat scale at home and the mobile device software can record specific values and perform calculations. MFSI had better performance than the other models for early MAFLD screening. The new model showed strong power and stability and shows promise in the area of MAFLD detection and self-assessment. The MRT was practical to assess disease alterations in real time.

Key words: Metabolic-associated fatty liver disease; Nonalcoholic fatty liver disease; Nonalcoholic steatohepatitis; Body fat mass; Waist-to-height ratio; Basal metabolic rate.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is regarded as an important cause of liver disease, affecting more than 25% of the general population worldwide; more than 50% of NAFLD patients also have dysmetabolism[1, 2]. In 2020, experts redefined NAFLD as MAFLD, and much emphasis was placed on the presence of metabolic-related diseases or dysfunction[3-5]. Researchers have found that MAFLD is a multisystem disease, and liver steatosis is associated with type 2 diabetes, chronic kidney disease, cardiovascular disease, and other diseases, which interact and form a vicious cycle[6-14]. China has the highest incidence of NAFLD/MAFLD morbidity in Asia[3, 15, 16]. Therefore, much attention should be given to MAFLD by enhancing awareness of MAFLD and optimizing its management.

To date, guidelines have suggested that liver biopsy could serve as the gold standard to diagnose histological liver damage, but the noninvasive quantitative assessment of liver fibrosis may also have prognostic implications. Ratziu et al.[17] collected liver biopsy samples from fifty-one patients and found that 41% of the patients were at different stages of liver fibrosis or had nonalcoholic steatohepatitis (NASH). The uneven distribution of histological lesions inevitably led to sampling error when performing biopsy. Abdominal imaging, such as B-ultrasound imaging and the controlled attenuation parameter (CAP) technique, can be used to diagnosis liver disease; the former is less sensitive to mild steatosis, while the latter can detect steatosis of more than 5% and is one of the most common noninvasive methods for quantifying hepatic steatosis and fibrosis clinically[18, 19]. The European Association for the Study of the Liver, European Association for the Study of Diabetes, and European Association for the Study of Obesity (EASL-EASD-EASO) updated the clinical practice guidelines, which propose that the NAFLD fibrosis score (NFS) and fibrosis-4 (FIB-4) index can be used as prognostic markers for the progression of liver disease[20]. The NFS has higher specificity in the elderly population (individuals aged > 65 years old)[21, 22]. The predictive performance of the NFS, FIB-4 index, and aspartate aminotransferase-to-platelet ratio index (APRI) has been consistent in relation to rates of liver-related disease and mortality but is less valuable for the prediction of liver fibrosis[23]. One study found that the combination of the NFS, FIB-4 index, and liver stiffness measurement (LSM) greatly improved the diagnostic accuracy, and the performance was similar to that of liver biopsy[24]. A cross-sectional study found that the triglyceride glucose (TyG) index was positively correlated with the likelihood and severity of NAFLD. The TyG index is generally considered a biomarker of steatosis, while its causal role in the judgement of fibrosis progression remains unclear[25, 26]. In addition, the hepatic steatosis index (HSI) is more accurate in discriminating between MAFLD and nonfatty liver disease than ultrasound. The predictive ability of the CAP for steatosis is superior to that of the HSI, and the HSI is more effective in discriminating moderate-to-severe patients[18, 27].

Studies have shown that numerous anthropometric indicators, such as the body mass index (BMI), waist-to-height ratio (WHtR), waist-hip ratio (WHR), and body adiposity index (BAI), are applicable for the quantification of visceral steatosis[28-32]. The body fat scale, a new popular domestic tool for health analysis, can be used to analyse basic parameters of body conditions such as the basal metabolic rate (BMR), body water distribution, and fat distribution. Reputable experts in the field have conducted extensive long-term studies on NAFLD/MAFLD, yet few noninvasive scoring models that accurately reflect disease activity or progression have been identified[33, 34].

Therefore, there is an urgent need to identify more accurate predictive indicators and develop new screening methods for early MAFLD screening. The aim of this study was to construct a noninvasive prediction system for MAFLD, explore this new system for early screening in public, and established a home-based tool for regular self-assessment and monitoring of MAFLD.

Methods

Study population

The participants came from Hangzhou, Shaoxing, Quzhou from March 2021 to November 2021, and a total of 2097 participants were enrolled (Figure 1). All participants signed the informed consent form and completed the examination as required. There were 1758 eligible participants in the training set who truthfully and completely answered the questionnaire, which contained items regarding height, weight, drinking history, past medical history and other basic information.

In order to validated the results of the raining set, there were two hundred eligible participants were grouped into the testing set.

All participants were diagnosed by LSM and were classified according to the CAP. A CAP value < 238 was considered to indicate healthy liver, 238 ≤ CAP value < 259 was considered to indicate mildly fatty liver, 259 ≤ CAP value < 292 was considered to indicate moderately fatty liver, and a CAP value ≥ 292 was considered to indicate severely fatty liver[35, 36].

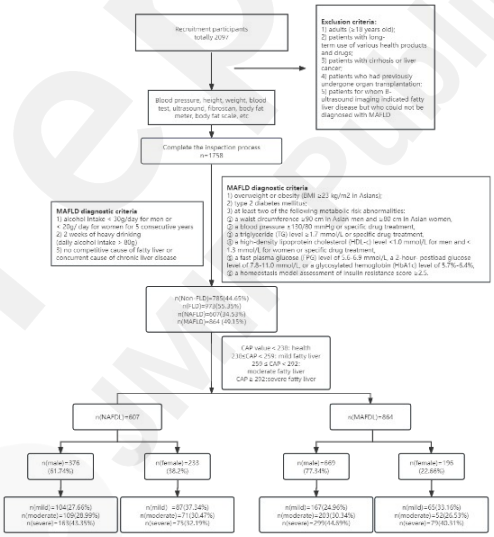

Figure 1: Flowchart about the inclusion process in the participants in training set, and the proportion of mild, moderate and severe fatty liver disease in NAFLD group and MAFLD group

Exclusion criteria

Patients who met the following criteria could not participate in this study: 1) adults (≥18 years old); 2) patients with long-term use of various health products and drugs; 3) patients with cirrhosis or liver cancer; 4) patients who had previously undergone organ transplantation; and 5) patients for whom B-ultrasound imaging indicated fatty liver disease but who could not be diagnosed with MAFLD.

Diagnostic criteria

The researchers in this study entered and organized the data, and the following diagnostic criteria were used to distinguish MAFLD patients[3]: 1) overweight or obesity (BMI ≥23 kg/m2 in Asians); 2) type 2 diabetes mellitus; and 3) at least two of the following metabolic risk abnormalities: ① a waist circumference ≥90 cm in Asian men and ≥80 cm in Asian women, ② a blood pressure ≥130/80 mmHg or specific drug treatment, ③ a triglyceride (TG) level ≥1.7 mmol/L or specific drug treatment, ④ a high-density lipoprotein cholesterol (HDL-c) level <1.0 mmol/L for men and 1.3 mmol/L for women or specific drug treatment, ⑤ a fast plasma glucose (FPG) level of 5.6-6.9 mmol/L, a 2-hour-postload glucose level of 7.8-11.0 mmol/L, or a glycosylated hemoglobin (HbA1c) level of 5.7%-6.4%, and ⑥ a homeostasis model assessment of insulin resistance score ≥2.5.

Data collection and model selection

All items were completed under the guidance of the researchers. The subjects underwent fasting blood tests. Waist circumference and hip circumference were measured with the participants wearing thin clothes. Body composition analysis was performed with bare feet. The patients were in a supine position during the FibroScan exam, and the right upper limb was held high and flat close to the ear. The probe was moved a small distance from the anchor point so that the most suitable detection point could be determined.

We collected basic information, including sex, age, height, weight, BMI, waist circumference, hip circumference, blood pressure, heart rate, and alcohol history. The following laboratory results were included: alanine aminotransferase (ALT), aspartate aminotransferase (AST), glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), haemoglobin, total cholesterol (TC), TG, HDL-c, low-density lipoprotein cholesterol (LDL-c), uric acid (UA), and FPG levels and white blood cell (WBC), red blood cell (RBC), and platelet (PLT) counts.

A body composition analyser (InBody770, Biospace, Seoul, Korea) was adopted to measure body composition and determine total body water (TBW), intracellular water (ICW), skeletal muscle mass (SMM), protein, and body fat mass (BFM). A body fat scale (3 Pro, Huawei, Shenzhen, China) was used to determine the BMR, Fat% and VFA.

The models or formulas involved in this study including BMI, FIB-4 index, Forns index score, APRI, glutamyl transpeptidase-to-platelet ratio index (GPR), HSI, and TyG index, were developed using the following standard equations:

BMI=weight/height2
FIB-4=age×AST/(PLT×√ALT)
Forns index score=7.811-3.131×In PLT(10E9/L)+0.781×In GGT+3.467×In age-0.014×TC
APRI= (AST/ULN)/PLT×100 (ULN: upper limit of normal)
GPR= (GGT/ULN)/PLT×100
HSI=8×(ALT/AST)+BMI (female+2, diabetes+2)
TyG=ln (TG×FPG/2)

Statistical analysis methods

Subjects were divided into the non-FLD group, which means healthy group, MAFLD group, and NAFLD group.

All data obtained in this study were analysed by SPSS statistical software version 26.0 (IBM

SPSS Statistics, Armonk, New York). The continuous variables were tested for normality and homogeneity of variance. A t test was performed for measurement data that followed a normal distribution, and the results are expressed as the mean±standard deviation. The nonnormally distributed data were analysed by nonparametric tests, and the results are represented by quartiles X (n, m). The chi-square test or Fisher's precision probability test was applied for quantitative data such as sex. Using ANOVA followed by post-hoc analysis tests to compare numerical data among the three groups (MAFLD, NAFLD, and non-FLD). P<0.01 indicated that the difference was statistically significant.

Binary logistic regression was performed to explore the potential anthropometric indicators with well predictive ability for screening MAFLD. A receiver operating characteristic (ROC) curve was drawn based on the selected indicators, and the area under the ROC curve (AUC) was calculated correspondingly. The indicator with the highest AUC was considered the most valuable indicator. The maximum Youden index (using the formula sensitivity + specificity -1) was used to define the optimal cut-off value. Potential confounding variables were added into the logistic regression equation step by step, including age, blood pressure, and FPG, TC, TG, HDL-c, and LDL-c levels. Calibration Model I (age, blood pressure and FPG level were added to the logistic regression equation) and Model II (age, blood pressure, and FPG, TC, TG, HDL-c, and LDL-c levels were added to the logistic regression equation) were established, and the predictive ability was evaluated before and after calibration. All significant indicators were included for the combination of diagnostic tests, and ROC curves were drawn. A new prediction model, the MAFLD Screening Index (MFSI), was constructed by logistic regression, and the model was validated in the testing set. All tests were two-tailed, and P<0.01 was considered statistically significant.

Ethical considerations

Every participant signed a written informed consent form and participated in the study anonymously. And it is impossible to individual participants in any images of manuscripts or other materials.

Every participant will be given an allowance of 300 RMB upon completion of the research project. The study protocol was approved by the Ethics Committee of Shulan Hangzhou Hospital. The approval number of the ethics approval form is NO. KY2021001.

The study did not involve additional invasive procedures, and there were no associated adverse reactions.

The data are not publicly available due to cooperative project clauses. Please contact author to inquire if date in this study is available for another studies.

Results

Comparing numerical data among the three groups (MAFLD, NAFLD, and non-FLD)

Using ANOVA analysis to compare the basic information and anthropometric indicators among three groups, the results showed that the all parameters with significant differences among MAFLD group, NAFLD group and non-FLD group. After post-hoc analysis tests, PLT counts (P=.099) had no significant differences between MAFLD group and non-FLD group, WBC counts (P=.255), TC (P=.350), LDL-c (P=.109), VFA (P=.065) and Fat% (P=.379) had no significant differences between MAFLD group and NAFLD group (table 1).

Table 1: Baseline characteristics and anthropometric indicators were compared in three groups ((MAFLD, NAFLD, and non-FLD)

	non-FLD (n=786)	MAFLD (n=864)	NAFLD (n=607)	F-Value H-Value X2-Value	P Value
Sex n (%)				224.985	<.001
Male	326 (41.5)	668 (77.3)	375 (61.8)		
Female	460 (58.5)	196 (22.7)	232 (38.2)		
Age (years)	36 (28-48)	45 (34-55)	40 (31-53)	107.212	<.001
Height (cm)	164.17±7.820	168.23±7.844	166.81±8.358	54.873	<.001
Weight (kg)	57.30 (51.60-64.30)	72.9 (66.2-80.7)	69.7 (61.1-78.1)	664.463	<.001
BMI (kg/m2)	21.49 (20.06-23.18)	25.66 (24.04-27.79)	25.04 (22.99-27.12)	798.113	<.001
SBP (mmHg)	119 (110-135)	132 (121-144)	128 (118-140)	218.758	<.001
DBP (mmHg)	74.89±11.216	82.88±11.863	79.72±11.611	91.652	<.001
WBCs(109/L)	5.80 (4.95-6.80)	6.5 (5.5-7.6)	6.3 (5.4-7.5)	91.944	<.001
RBCs (1012/L)	4.69 (4.39-5.11)	5.12 (4.81-5.42)	5.02 (4.65-5.38)	210.018	<.001
Hb (g/L)	140 (131-153)	155 (145-163)	150 (137-160)	213.919	<.001
PLTs (109/L)	234.66±55.331	238.18±58.518	244.67±58.671	5.041	.006
FPG (mmol/L)	4.60 (4.36-4.89)	4.88 (4.55-5.34)	4.80 (4.50-5.19)	128.314	<.001
ALT (U/L)	14 (10-20)	27.00 (19.00-34.00)	24.00 (17.75-40.00)	475.850	<.001
AST (U/L)	20 (17-24)	25.00 (21.00-32.00)	24.00 (19.00-29.00)	245.274	<.001
ALP (U/L)	57 (47-70)	69.00 (57.00-83.00)	66.00 (55.00-81.00)	146.960	<.001
GGT (U/L)	15 (12-21)	31.00 (20.00-52.00)	24.00 (17.00-38.00)	496.679	<.001
TC (mmol/L)	4.71 (4.13-5.23)	4.99 (4.38-5.33)	4.96 (4.33-5.55)	47.740	<.001
TGs (mmol/L)	0.93 (0.71-1.26)	1.76 (1.21-2.45)	1.49 (1.07-2.24)	529.457	<.001
HDL-c (mmol/L)	1.48 (1.28-1.68)	1.21 (1.07-1.40)	1.26 (1.07-1.45)	284.363	<.001
LDL-c (mmol/L)	2.64 (2.23-3.16)	3.10 (2.64-3.64)	3.04 (2.56-3.55)	146.926	<.001
UA (μmol/L)	295.99±80.86	378.82±85.081	358.39±87.676	206.430	<.001
E-Value (kPa)	4.40 (3.70-5.20)	5.2 (4.3-6.3)	5.0 (4.2-6.0)	164.275	<.001
CAP (dB/m)	200 (179-218)	284 (257-320)	278 (255-315)	1538.285	<.001
WHtR	0.459±0.0656	0.524±0.5117	0.512±0.0984	113.769	<.001
WHR	0.829 (0.783-0.880)	0.918 (0.872-0.950)	0.892 (0.840-0.939)	284.420	<.001
FIB-4 index	0.813 (0.588-1.234)	0.954 (0.608-1.362)	0.782 (0.521-1.235)	15.698	<.001
Forns index	5.471±1.6797	6.536±1.5977	6.005±1.6630	166.437	<.001
APRI	0.240 (0.187-0.301)	0.282 (0.215-0.376)	0.263 (0.201-0.351)	72.070	<.001
GPR	0.133 (0.103-0.192)	0.230 (0.159-0.403)	0.186 (0.135-0.292)	325.345	<.001
HSI	28.57 (26.31-30.84)	35.28 (32.02-39.04)	34.47 (30.87-38.63)	772.797	<.001
TyG index	8.137 (7.863-8.463)	8.855 (8.463-9.234)	8.674 (8.322-9.092)	585.116	<.001
TBW	30.30 (27.2-036.40)	38.65 (33.80-42.90)	36.85 (30.23-42.88)	341.198	<.001
ICW	18.80 (16.70-22.60)	24.10 (20.90-26.80)	22.80 (18.70-26.10)	340.014	<.001
Protein	8.10 (7.20-9.80)	10.40 (9.08-11.60)	9.90 (8.10-11.30)	339.536	<.001
BFM	14.90 (12.00-17.40)	20.80 (17.60-24.43)	20.10 (16.80-24.20)	638.768	<.001
SMM	22.50 (19.80-27.53)	29.40 (25.30-32.93)	27.80 (22.35-32.10)	336.593	<.001
BMR (kcal)	1283.95 (1179.70-1450.17)	1526.55 (1387.09-1655.52)	1470.15 (1276.65-1622.62)	358.763	<.001
VFA	6.552 (5.235-7.762)	9.013 (7.598-10.813)	8.753 (7.294-10.671)	518.559	<.001

Fat (%)	25.319±5.9566	28.255±5.2256	28.524±5.7358	68.099	<.001

Predictive performance of different anthropometric indicators

The above variables with *P*<0.01 were further included in the logistic regression. The ROC curves and optimal cut-off points for the selected indicators are shown in Table 2 and Figure 2. The AUCs of the WHtR, the Forns index, the HSI, the TyG index, TBW, BFM, and BMR were 0.866, 0.684, 0.873, 0.835, 0.760, 0.842, and 0.778 respectively (*P*<.001) (Table 2).

According to the ROC curve and AUC (Figure 2), the HSI had the strongest predictive performance for MAFLD in the training set, and the performance ranking was as follows: the HSI, the WHtR, BFM, the TyG index, TBW, and the Forns index. The confounding factors were further corrected for in logistic regression (Model I: age, blood pressure and the FPG level were added to the logistic regression equation; Model II: age, blood pressure, and FPG, TC, TG, HDL-c, and LDL-c levels were added to the logistic regression equation). After correction for confounding factors, the odds ratio (OR) of the Forns index in Model I was 1.043 (95% CI: 0.851-1.277), and that in Model II was 1.050 (95% CI: 0.854-1.293) (Table 3). The results showed that the performance of the Forns index for MAFLD screening was unstable, and the performance of other anthropometric indicators was not easily influenced by confounders.

The HSI and WHtR showed better predictive performance than the other indicators. The sensitivity of the HSI was higher than that of the other anthropometric indicators (sensitivity: 81.4%), and the specificity of the WHtR was higher than that of the other anthropometric indicators (specificity: 79.8%). The combination of the WHtR, the HSI and BFM increased the predictive ability for MAFLD, and the AUC was 0.900 (specificity: 81.8%, sensitivity: 85.6%, *P*<.001) (Table 2).

Table2: Cut-off points and AUCs (95% CIs) were used to demonstrate the screening ability of the different anthropometric indicators for MAFLD (n=1649)

	AUC (95% CI)	P Value	Cut-off point	Specificity (%)	Sensitivity (%)
WHtR	0.866	<.001	0.501449713	79.8	80.8
Forns index	0.684	<.001	6.160599276	67.8	61.3
HSI	0.873	<.001	31.15061285	76.8	81.4
TyG index	0.835	<.001	8.450341708	74.0	76.5
TBW	0.760	<.001	36.55	75.3	65.3
BFM	0.842	<.001	17.55	76.9	76.2
BMR	0.778	<.001	1434.263124	73.1	70.1
Combination (WHtR/HSI)	0.885	<.001	/	76.0	85.6
Combination (WHtR/BFM)	0.881	<.001	/	81.7	80.0
Combination (BFM/HSI)	0.889	<.001	/	81.0	82.9
Combination (WHtR/HSI/BFM)	0.900	<.001	/	81.8	85.6

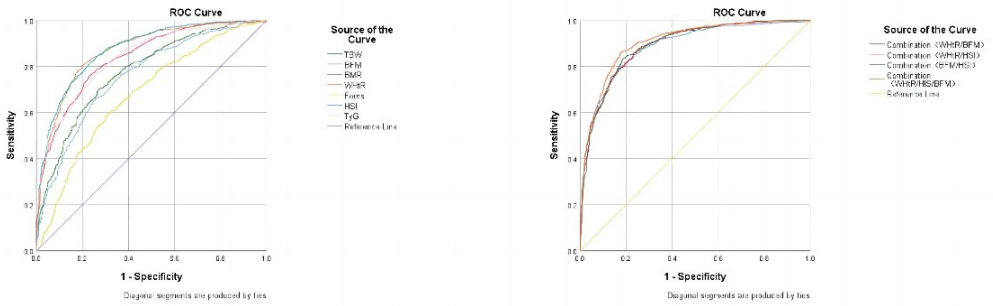

Figure 2: ROC curves showed the screening ability of different anthropometric indicators for MAFLD

Table 3: Confounders were corrected by binary logistic regression to compare changes in screening power for different anthropometric indicators (n=1649)

	Nonadjusted		Model I		Model II	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
TBW	1.079 (1.051-1.109)	<.001	1.086 (1.055-1.118)	<.001	1.075 (1.042-1.108)	<.001
BFM	1.255 (1.194-1.319)	<.001	1.250 (1.186-1.317)	<.001	1.257 (1.192-1.326)	<.001
WHtR	145.540 (9.015-2349.524)	<.001	107.825 (6.232-1865.456)	.001	113.408 (6.759-1902.900)	<.001
Forns index	1.166 (1.053-1.292)	.003	1.043 (0.851-1.277)	.685	1.050 (0.854-1.293)	.642
HSI	1.124 (1.070-1.182)	<.001	1.128 (1.070-1.190)	<.001	1.110 (1.052-1.172)	<.001
TyG index	6.557 (4.560-9.427)	<.001	5.832 (3.972-8.562)	<.001	6.005 (3.764-9.579)	<.001

Development of a new MAFLD screening model

The HSI, the WHtR and BFM displayed strong power in screening for MAFLD. The HSI was calculated based on BMI, ALT levels and AST levels and was not suitable for early screening for MAFLD. The purpose of establishing a new model was to reduce the need for invasive procedures and reduce the frequency of medical visits, as well as to screen for MAFLD in high-risk populations. The predictive ability of TBW was stable after correcting for confounders (95% CI in Model I: 1.055-1.118, 95% CI in Model II: 1.042-1.108) (Table 3). So TBW was included in the new model. Logistic regression was applied to establish the MAFLD early screening model, which was named the MFSI. The formula was as follows: MFSI= -13.968+0.120×TBW+0.254×BFM+10.793×WHtR (Figure 3). The AUC of the MFSI was 0.896 (specificity: 83.8%, sensitivity: 82.1%) (*P*<.001) (Table 4). Collectively, the performance between the MFSI and the WHtR/HSI/BFM combination model was similar.

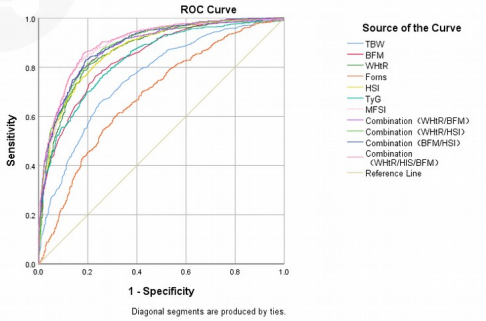

Figure 3: ROC curves showed the screening ability of different combination of anthropometric indicators and the new MAFLD screening model named MFSI (MFSI= -

13.968+0.120×TBW+0.254×BFM+10.793×WHtR)

Table 4: Cut-off points and AUCs (95% CIs) were used to compared the screening ability of different anthropometric indicators and the MFSI (n=1649)

	AUC (95% CI)	P Value	Cut-off point	Specificity (%)	Sensitivity (%)
WHtR	0.866	<.001	0.501449713	79.8	80.8
Forns index	0.684	<.001	6.160599276	67.8	61.3
HSI	0.873	<.001	31.15061285	76.8	81.4
TyG index	0.835	<.001	8.450341708	74.0	76.5
TBW	0.760	<.001	36.55	75.3	65.3
BFM	0.842	<.001	17.55	76.9	76.2
Combination (WHtR/HSI)	0.885	<.001	/	76.0	85.6
Combination (WHtR/BFM)	0.881	<.001	/	81.7	80.0
Combination (BFM/HSI)	0.889	<.001	/	81.0	82.9
Combination (WHtR/HSI/BFM)	0.900	<.001	/	81.8	85.6
MFSI	0.896	<.001	0.5146795	83.8	82.1

Performance of the MFSI in the testing set

There were further 200 participants enrolled in the testing set, including 51 non-FLD patients and 149 MAFLD patients. To evaluate the predictive ability of the MFSI for screening for MAFLD in a high-risk population, the MFSI was applied to the testing set, and ROC curves were drawn based on the MFSI, BFM, the WHtR, the HSI, TBW, and the WHtR/HSI/BFM combined model (Figure 4). The AUC (testing set) of the MFSI was 0.917, the specificity was 89.8%, and the sensitivity was 84.4%, and the AUC (testing set) of the WHtR/HSI/BFM combined model was 0.920, the specificity was 89.8%, and the sensitivity was 81.6% (Table 5). The performance of the MFSI was similar to that of the WHtR/HSI/BFM combined model in the testing set.

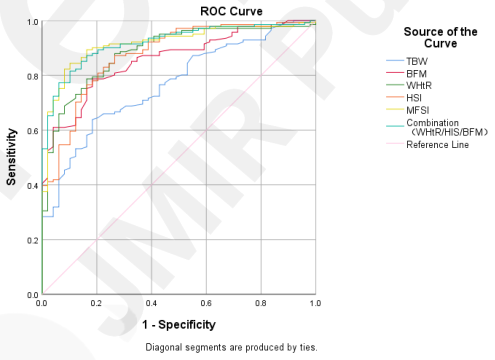

Figure 4: ROC curves showed the screening ability of different anthropometric indicators and MFSI in the testing set

Table 5: AUCs (95% CIs) were used to compare the different anthropometric indicators and the MFSI in screening for MAFLD in testing set (n=200)

	AUC (95% CI)	P Value	Specificity (%)	Sensitivity (%)
WHtR	0.886	<.001	83.7	78.7
TBW	0.767	<.001	81.6	63.8
BFM	0.858	<.001	81.6	78.7
HSI	0.877	<.001	73.5	87.2
Combination (WHtR/HSI/BFM)	0.920	<.001	89.8	81.6
MFSI	0.917	<.001	89.8	84.4

MAFLD Rating Table: MRT, for prediction MAFLD

The scoring system based on the MFSI and the application program was more practical for patient self-assessment. The MRT also included TBW, BFM, and the WHtR. An MRT score ranging from 0-2 indicated health, and a score≥3 indicated MAFLD (Table 6). The AUC of the MRT for MAFLD prediction was 0.876 (*P*<.001) (Figure 5).

Table 6: Simple rating table to assess risk factors for MAFLD

	0	1	2	3	4
TBW	<33.35	33.35-45.05	≥45.05		
BFM	<17.55	17.55-20.15	10.15-22.95	≥22.95	
WHtR	<0.501		0.501-0.525	0.525-0.538	≥0.538

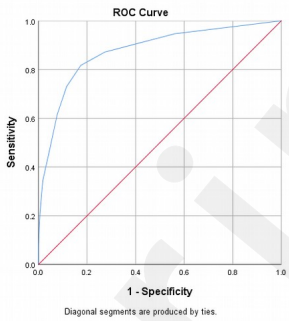

Figure 5: ROC curves of the MRT showed the correlation with MAFLD and the AUC for MAFLD prediction was 0.876 (*P*<.001)

Discussion

The WHtR, BFM, and TBW were predictors of MAFLD. The AUC of the WHtR was 0.866 (specificity: 79.8%, sensitivity: 80.8%), the AUC of BFM was 0.842 (specificity: 76.9%, sensitivity: 76.2%), and the AUC of TBW was 0.760 (specificity: 75.3%, sensitivity: 65.3%). The novel MFSI model, derived through logistic regression, included the WHtR, BFM, and TBW. Notably, the MFSI demonstrates independence from laboratory findings. Upon validation, it was observed that the MFSI exhibited stability while offering advantages in terms of sensitivity and specificity for MAFLD screening (AUC in the training set: 0.896, specificity: 83.8%, sensitivity: 82.1%, AUC in the testing set: 0.917, specificity: 89.8%, sensitivity: 84.4%).

Researchers found that the measurement of visceral fat can predict the occurrence of chronic diseases, such as diabetes, hyperuricaemia, and metabolic syndrome[37, 38]. NAFLD/MAFLD affects more than 25% of the global population and are considered different stages of the disease course. Because of long-term subtle inflammation and unobvious clinical manifestations, some patients gradually develop liver fibrosis and cirrhosis[1]. It is important to raise the awareness of the population and optimize the management of this disease.

In recent decades, researchers have considered that the APRI, FIB-4 index, BMI, HSI, and TyG index have high accuracy for the diagnosis of liver fibrosis. Nonfibrosis scores were higher in patients with MAFLD than in those with NAFLD[11, 39-42]. Similar conclusions were drawn in the present work. To distinguish MAFLD patients in the population, we compared traditional indicators and body composition between the MAFLD group and the non-FLD group and found that there was a significant difference between the two groups. Although traditional indicators had efficient performance for the prediction of liver fibrosis, it was doubtful that these indicators were robust for the screening of MAFLD before being confirmed by histological liver

examination. The previously published work mainly focused on the predictive ability of indicators for the detection of liver fibrosis, while much work omitted the performance of these indicators for the early screening of MAFLD.

Lee's group put forward a new indicator named the HSI, and they found that NAFLD cannot be diagnosed when the HSI was <30.0, with a sensitivity of 92.5% (95% CI, 91.4-93.5)[27]. The HSI showed a similar performance for MAFLD diagnosis in this study. Italian researchers proposed another new indicator, the fatty liver index (FLI), which is calculated based on waist circumference, BMI, TG levels, and GGT levels. When the FLI is <30, the diagnosis of fatty liver disease can be ruled out, and when the FLI is ≥60, patients be diagnosed with fatty liver disease. Waist circumference and BMI are the most robust predictors for the screening of fatty liver disease[43]. In contrast to the HSI, the FLI was established by incorporating waist circumference. However, the BMI and waist circumference were totally different for people with varied dietary habits, and the study did not take this into account. Zhang's group found that the WHtR had great performance for MAFLD screening, with a sensitivity of 96% and specificity of 64%[44]. In our study, the WHtR showed a sensitivity of 80.8% and specificity of 79.8% for MAFLD screening.

TG and FPG levels are considered the two pivotal inducers of metabolic syndrome. TGs are produced excessively in the process of fat accumulation, and insulin resistance accelerates hepatic steatosis. The TyG index can be used as a simple alternative marker for the detection of insulin resistance in the diagnostic test combining TG and FPG levels. The prevalence and severity of MAFLD were positively correlated with the TyG index[25, 45-47]. The AUC of the TyG index for predicting MAFLD was 0.835 (95% CI: 4.560-9.427), which might be valuable for clinical practice.

A meta-analysis revealed that the visceral adiposity index (VAI) was an independent predictor of MAFLD, which could be used to predict potential morbidity[48]. However, the predictive ability of the VAI has not been verified. Wang et al.[49] found that nonobese MAFLD patients had higher BFM and VFA values than the healthy population, and most of them had abnormal lipid metabolism. In addition, BFM and VFA were valuable for distinguishing MAFLD patients from nonobese people[49, 50]. This conclusion was also confirmed in the present study (AUC of BFM for the prediction of MAFLD was 0.842; sensitivity: 76.2%, specificity: 76.9%).

This study aimed to establish a home-based model for early screening of MAFLD to promote disease self-assessment and management. Compared with previously published models that rely heavily on laboratory indicators, our model combined body composition and the WHtR for the screening of MAFLD, the body parameters that was used to build screening model can be easily obtained by body fat scale at home. The mobile device software can record specific values and perform calculations.

There were two significant advantages of our model: 1) the need for invasive examination was reduced and medical expenditures were less, 2) early screening models can provide early warning signs of disease, prompting people to modify diet and exercise or seek medical treatment if necessary, 3) enhance patient and physician interaction.

There were also some limitations of our present work. First, this study was limited by geographical factors, and regional bias existed. Second, due to ethical considerations, the results in this study cannot be confirmed by histological liver examination. Third, we often

enter some villages for recruitment, we are unable to obtain radiological diagnosis due to manpower, transportation and other constraints. What's more, it was also difficult to follow up participants who underwent physical examination in different areas, and the re-examination data could not be compared with previous data.

Although our study found that the new MFSI model and MRT were valuable for MAFLD prediction, the diagnosis of the disease still requires experienced clinicians, and those with disease or high risk should seek medical attention in time.

Acknowledgements

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Conflicts of interest

None declared

Abbreviations

ALT: alanine aminotransferase
ALP: alkaline phosphatase
AUC: area under the ROC curve
AST: aspartate aminotransferase
APRI: aspartate aminotransferase-to-platelet ratio index
BMR: basal metabolic rate
BAI: body adiposity index
BFM: body fat mass
VFA: body fat mass (BFM), visceral fat area
BMI: body mass index
CAP: controlled attenuation parameter
EASL-EASD-EASO: European Association for the Study of Obesity
FPG: fast plasma glucose
FLI: fatty liver index
FIB-4: fibrosis-4
GGT: glutamyl transpeptidase
GPR: glutamyl transpeptidase-to-platelet ratio index
HbA1c: glycosylated hemoglobin
HSI: hepatic steatosis index
HDL-c: high-density lipoprotein cholesterol)
ICW: intracellular water
LSM: liver stiffness measurement
LDL-c: low-density lipoprotein cholesterol)
MAFLD: Metabolically associated fatty liver disease
NFS: NAFLD fibrosis score
NAFL1: D Nonalcoholic fatty liver disease
NASH: nonalcoholic steatohepatitis
OR: odds ratio
PLT: platelet

ROC: receiver operating characteristic
RBC: red blood cell
SMM: skeletal muscle mass
TBW: total body water
TC: total cholesterol
TG: triglyceride
TyG: triglyceride glucose
UA: uric acid
VAI: visceral adiposity index
VFA: visceral fat area
WHR: waist-hip ratio
WHtR: waist-to-height ratio
WBC: white blood cell

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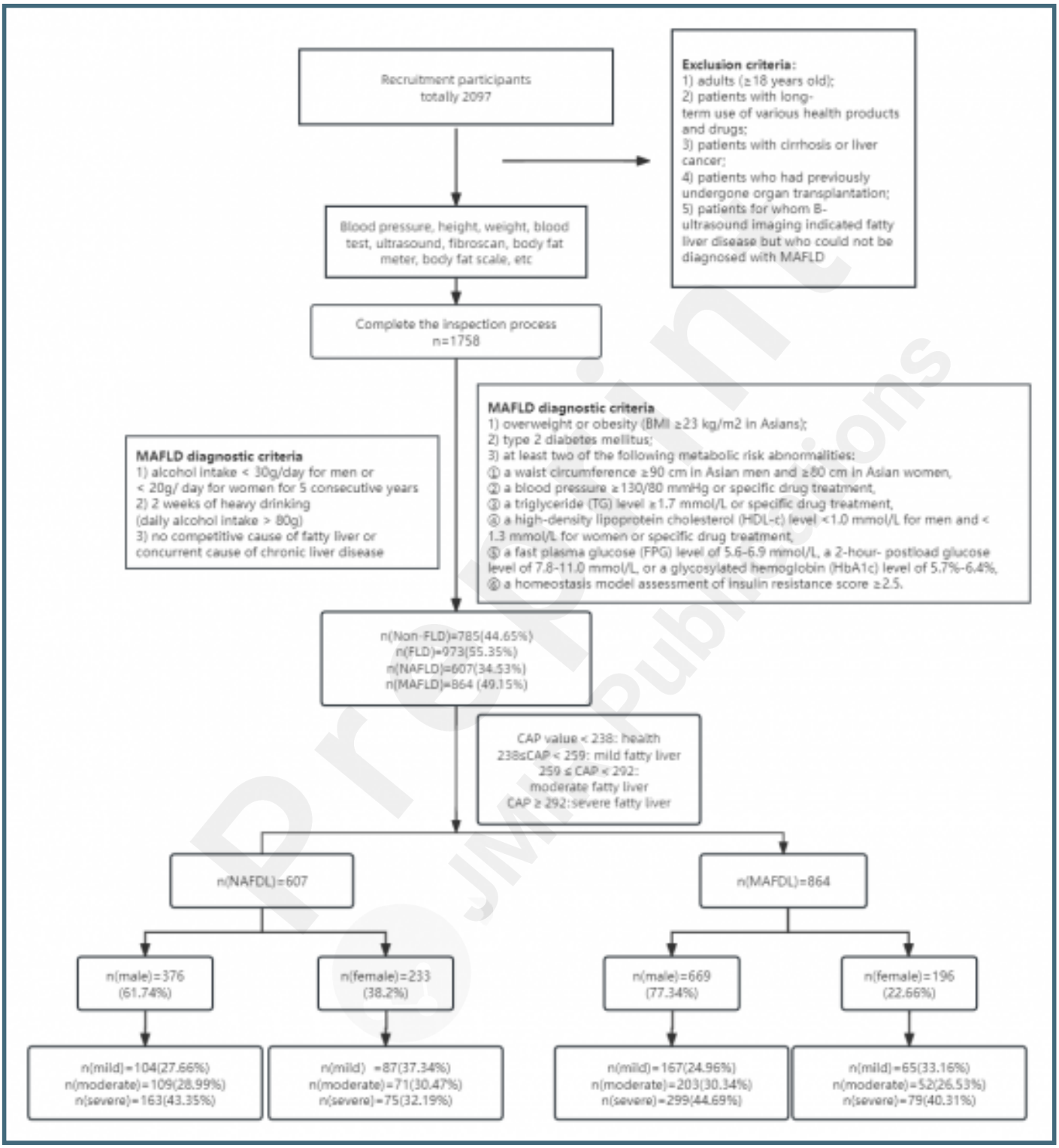
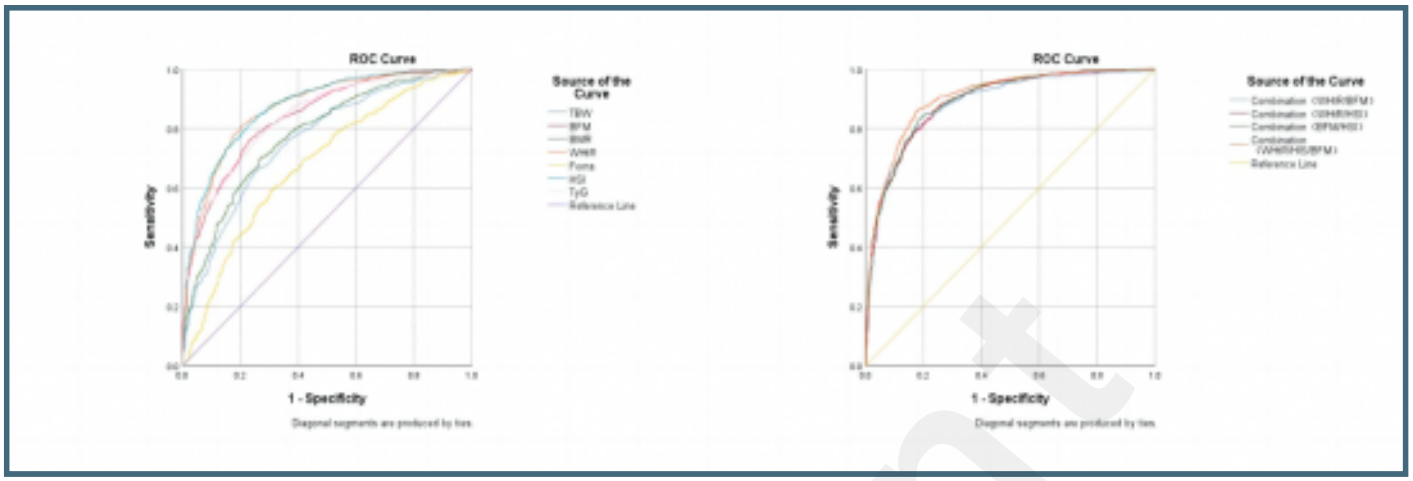
Supplementary Files

Figures

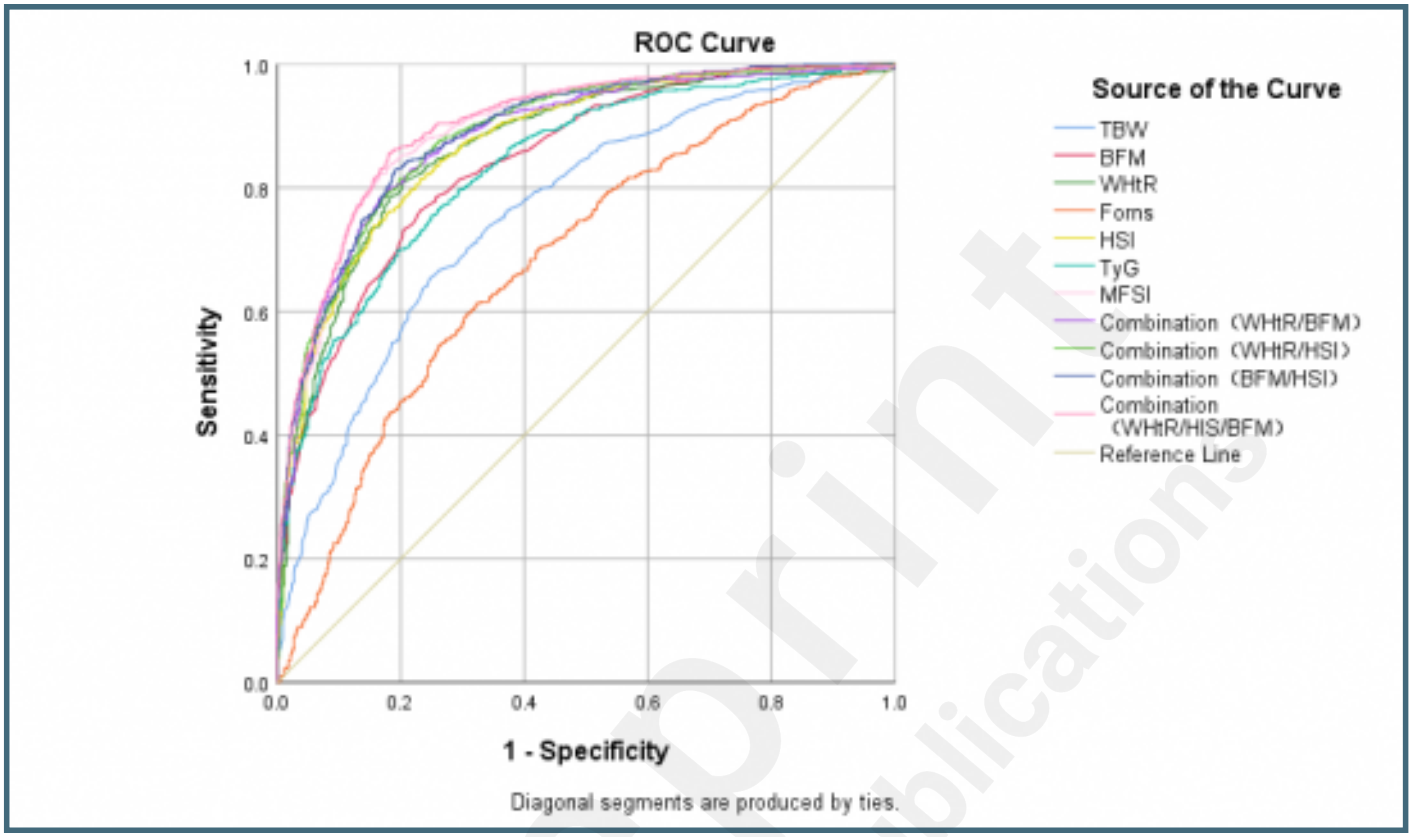
Flowchart about the inclusion process in the participants in training set, and the proportion of mild, moderate and severe fatty liver disease in NAFLD group and MAFLD group.



ROC curves showed the screening ability of different anthropometric indicators for MAFLD.



ROC curves showed the screening ability of different combination of anthropometric indicators and the new MAFLD screening model named MFSI (MFSI= -13.968+0.120×TBW+0.254×BFM+10.793×WHtR).



ROC curves showed the screening ability of different anthropometric indicators and MFSI in the testing set.