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ORIGINAL RESEARCH

Predictive Value of the Chinese Visceral Adiposity Index for Metabolic Dysfunction-Associated Fatty Liver Disease and Elevated Alanine Aminotransferase Levels in Nonobese Chinese Adults: A Cross-Sectional Study

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Purpose: It is unclear how the Chinese Visceral Adiposity Index (cVAI) relates to metabolic dysfunction-associated fatty liver disease (MAFLD) and alanine aminotransferase (ALT) in nonobese individuals. In this study, we evaluated the ability of the cVAI to predict MAFLD and elevated ALT in nonobese participants.

Methods: This cross-sectional study recruited 541 nonobese subjects from March 2019 to January 2022 with the age range of 18–80 years. Hepatic steatosis was diagnosed by ultrasound. Participants were divided into four groups according to cVAI quartiles. To assess the associations between cVAI and MAFLD and elevated ALT, multivariate logistic regression was used. Receiver operating characteristic (ROC) curves were generated to evaluate the ability of the cVAI to predict MAFLD and elevated ALT.

Results: Compared to the group with the lowest cVAI, the group with the highest cVAI was positively associated with nonobese MAFLD [16.173 (4.082–64.073), $P < 0.001$] and elevated ALT [8.463 (2.859–25.049), $P < 0.001$]. The area under the ROC curve (AUC) of the cVAI was greater than that of WC, waist-to-height ratio, or BMI for predicting nonobese MAFLD in the male, female, > 38 and ≤ 38 years old subgroups ($P < 0.05$), respectively. In addition, the ability of the cVAI to predict MAFLD was better in females, young individuals, and individuals with a higher education level ($P < 0.05$). The cVAI also had good predictive ability for elevated ALT levels [0.655 (0.602–0.708)], particularly in females, young people, and highly educated participants. Furthermore, the cVAI was strongly positively correlated with the liver fibrosis score ($P < 0.05$) and was also a strong indicator of concomitant metabolic syndrome in nonobese MAFLD patients [AUC = 0.688 (0.612–0.763)].

Conclusion: The cVAI was strongly related to nonobese MAFLD and elevated ALT. The cVAI may be a reliable and accessible predictor of nonobese MAFLD and elevated ALT.

Keywords: Chinese visceral adiposity index, metabolic dysfunction-associated fatty liver disease, nonobese, Chinese, cross-sectional study

Introduction

In 2020, the term metabolic dysfunction-associated fatty liver disease (MAFLD) was used in place of nonalcoholic fatty liver disease (NAFLD).[1,2] MAFLD has superior utility in identifying patients at high risk for metabolic dysfunction and

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hepatic and extrahepatic complications,[3] and the definition has now been promoted globally.[4] The prevalence of MAFLD has increased over the past decade due to lifestyle changes and ambient air pollution.[5] Globally, MAFLD has been identified as the major cause of chronic liver disease, especially within China, where it currently accounts for thirty percent of cases.[6] The prevalence of MAFLD increases with age, and patients are predominantly male.[7] Without intervention, MAFLD can progress to steatohepatitis, hepatic fibrosis, and ultimately liver tumors.[1,2,8] Furthermore, MAFLD represents a multisystem disease that is strongly related to cancer, chronic kidney disease, and cardiovascular disease.[8,9] Given that metabolic syndrome (MS) is the key factor underlying MAFLD, it is reasonable to infer that other diseases closely associated with MS are also related to MAFLD.[10] MAFLD has emerged as an enormous financial burden and is now an increasing worldwide health issue.

Liver biopsy is the most accurate method for diagnosing fatty liver, but patient compliance is poor due to the invasion and difficulty involved. Both computed tomography (CT) and magnetic resonance imaging (MRI) have good diagnostic efficacy for fatty liver but cannot be used for widespread screening due to the radiation and high cost involved.[11] Therefore, the search for novel and convenient diagnostic methods is extremely urgent. Although MAFLD is typically associated with obesity, there is increasing evidence that people with normal weight could also develop fatty liver.[12] A meta-analysis covering 10,576,000 subjects revealed that approximately 40% of patients with fatty liver globally were nonobese.[13] According to a recent research, people with fatty livers who were slim were almost as likely to develop steatohepatitis and cirrhosis as were those who were overweight or obese.[14] Additionally, nonobese MAFLD patients are at increased risk of being missed. Therefore, identifying a useful and easy indicator of the prognosis of nonobese MAFLD patients is extremely critical.[12,15]

There is substantial evidence that the distribution of adipose tissue is important for the onset and progression of MAFLD.[16,17] The Chinese Visceral Adiposity Index (cVAI), created by Xia et al[18] specifically for Asian populations, measures visceral adiposity. Thereafter, various investigations have suggested significant relationships between cVAI and metabolism disorders, such as type 2 diabetes mellitus (T2DM), hypertension, and carotid plaque.[19–21] A few studies have reported that the cVAI could also be used as an independent predictive indicator in the diagnosis of fatty liver.[22,23] Our preliminary study revealed that the cardiometabolic index and atherogenic index of plasma, indicators of visceral adipose tissue, had far greater predictive value for nonobese MAFLD individuals than for obese MAFLD individuals.[11,24] However, it is unclear whether the cVAI has a similar predictive value for nonobese MAFLD individuals. Additionally, alanine aminotransferase (ALT) is a widely used indicator of hepatic impairment, although few articles have reported the connection between ALT and the cVAI. Consequently, it is unclear how the cVAI affects ALT levels.[25]

Accordingly, the present investigation sought to systematically examine the correlation between cVAI and MAFLD and elevated ALT in nonobese participants and investigate the predictive value of the cVAI for the early detection and management of nonobese MAFLD and hepatic impairment.

Methods and Materials

Study Design and Participants

This cross-sectional study was performed in Beijing, China, and approved by the Ethics Committee of Clinical Research of China-Japan Friendship Hospital (Approval No.: 2018–110-K79-1). The study sample of 864 participants was derived from two of our previously published articles,[11,24] which were included from China-Japan Friendship Hospital from March 2019 to January 2022 with the age range of 18–80 years. These participants complied with a standardized survey, and undertook physical examinations and laboratory testing continuously. All the participants consented to willingly join this study and signed the informed consent forms.

After excluding 1) patients with other causes of liver disease such as alcohol consumption, viruses, autoimmune diseases, etc; 2) pregnant or breastfeeding women; 3) those with severe neurological, cardiovascular, respiratory, digestive, urinary, or haematological diseases; 4) those with mental diseases, infectious diseases, connective tissue diseases, or malignant tumors; 5) those whose body mass index (BMI) $\geq$ 28.00 kg/m$^{2;}$ 6) those whose data were incomplete, 541 subjects were recruited—including 188 subjects in the MAFLD group and 353 subjects in the non-MAFLD group (Figure 1).

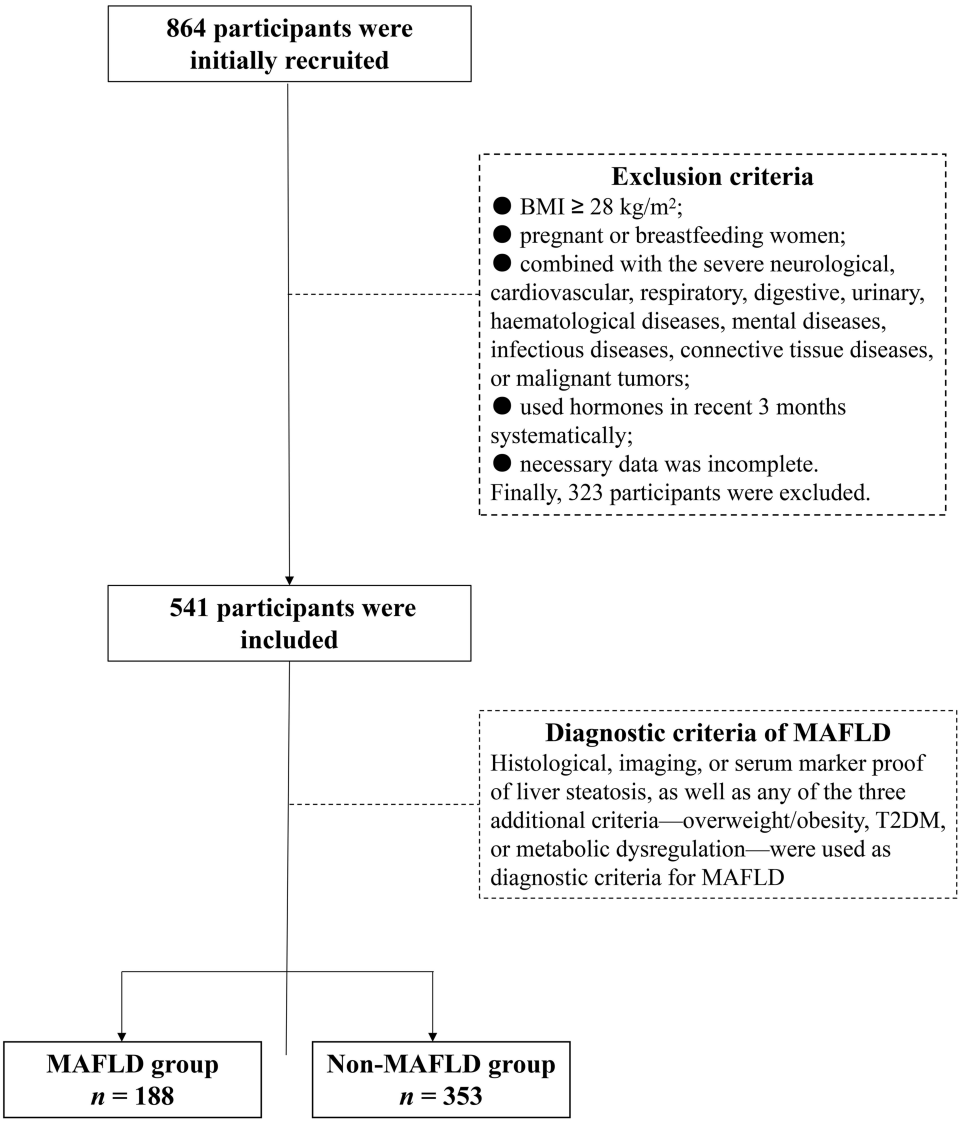


Figure 1 Flowchart of the study.
Abbreviations: BMI, body mass index; MAFLD, metabolic dysfunction-associated fatty liver disease.

Diagnostic Criteria for MAFLD

Imaging proof of liver steatosis, as well as any of the three additional criteria—overweight/obesity, T2DM, or metabolic dysregulation—were used as diagnostic criteria for MAFLD.[1] Hepatic steatosis was diagnosed by ultrasound in all patients. Abdominal ultrasonography was conducted by a skilled sonographer to assess hepatic steatosis. A diagnosis of hepatic steatosis can be made by meeting two of the following three criteria: diffuse enhancement of ultrasound echo in the liver near-field, liver echo greater than the kidney, vascularity blurring and gradual attenuation of far-field ultrasound echo.[26]

Diagnostic Criteria for MS

The diagnosis of MS involves the fulfillment of three or more criteria for metabolic abnormalities: 1) waist circumference (WC) ≥ 102/88 cm in men or women; 2) blood pressure ≥ 130/85 mmHg; 3) high-density lipoprotein cholesterol (HDL-C) < 40/50 mg/dl for men or women; 4) triglycerides (TG) ≥ 150 mg/dl; and 5) fasting glucose ≥ 100 mg/dL.[27]

Collected Data

Basic Information and Measurement Indicators

Professionally qualified researchers collected the subjects' basic information (sex, age, history, etc.) and measurement indices (height, weight, WC, and blood pressure) using standard questionnaires and relevant measurement instruments. Drinking history was defined as consumption of one standard alcoholic beverage at least once a week or more for at least 6 months. Smoking history was defined as more than 10 cigarettes per week for at least 6 months.[28] Researchers told the participants to take off shoes, coats, and other heavy objects, stand upright, look straight ahead, not look up or down, and naturally stand on the measuring instrument, measuring their height, and weight. In the meanwhile, the participants were asked to stand naturally, not take their abdomen, and their breathing remained stable The WC was measured with a ruler around the flat navel level. Then, blood pressure was measured using an upper-arm electronic sphygmomanometer. Participants were asked to sit still, relax their bodies, remove thicker clothes on their arms, wear the cuff of the sphygmomanometer, palm up, and keep their palms and chests on the same horizontal line. During the measurement, the participants should not talk or move their bodies, while researchers took the average value three times to obtain systolic blood pressure (SBP) and diastolic blood pressure (DBP).

Laboratory Indicators

The laboratory indices were available via the online file system of the medical examination center. Blood samples were obtained after an overnight fast to measure plasma TG, total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), aspartate aminotransferase (AST), ALT, fasting blood glucose (FBG), and serum uric acid (SUA) levels. Biochemistry assays were performed using standardized methods in the Laboratory of China-Japan Friendship Hospital.[29] According to the 9th edition of Diagnostics published by the China Press of Traditional Chinese Medicine, > 40 U/L was the cutoff for elevated ALT and AST levels, elevated TC was defined as TC ≥ 5.18 mmol/L, elevated TG was defined as TG ≥ 1.70 mmol/L, decreased HDL-C was defined as HDL-C < 1.04 mmol/L, elevated LDL-C was defined as LDL-C ≥ 3.37 mmol/L, elevated FBG was defined as FBG > 6.10 mmol/L, and SUA > 416/357 μmol/L for men/women was the cutoff for hyperuricemia.[30]

Calculated Indicators

Based on the above indexes, BMI = body weight (kg)/height squared (m^2); waist-to-height ratio (WHtR) = WC (cm)/height (cm);[31] cVAI (male) = $-267.93 + 0.68 \times$ age (years) $+ 0.03 \times$ BMI (kg/m^2) $+ 4.00 \times$ WC (cm) $+ 22.00 \times$ log10TG (mmol/L) - $16.32 \times$ HDL-C (mmol/L), cVAI (female) = $-187.32 + 1.71 \times$ age (years) $+ 4.23 \times$ BMI (kg/m^2) $+ 1.12 \times$ WC (cm) $+ 39.76 \times$ log10TG (mmol/L) - $11.66 \times$ HDL-C (mmol/L).[18] The NAFLD fibrosis score (NFS) was calculated as $-1.675 + 0.037 \times$ age (years) $+ 0.094 \times$ BMI (kg/m^2) $+ 1.13 \times$ impaired fasting glucose/T2DM (yes = 1, no = 0) $+ 0.99 \times$ AST/ALT ratio - $0.013 \times$ platelet (10^9/L) - $0.66 \times$ albumin (g/dL).[32]

Statistical Analysis

The arithmetic mean and standard deviation (%*MathType*!*Translator*!2!1!*PlainTeX.tdl*!*PlainTeX*!$\bar{x}$%*MathType*!*End*!2!1! ± SD) of the normally distributed quantitative data were provided, and the *t* test was used to compare the two groups. Quantitative data conforming to a nonnormal distribution were presented as M (P_{25}, P_{75}), and Wilcoxon rank sum tests were used to compare the two groups. The qualitative data were presented as the number of patients and percentage, and the χ^2 test was used to compare the two groups. Spearman correlation analysis was carried out to investigate the correlations between predictors and biochemical indices, and the results were made into a heatmap.

Four groups were created from the participants using the cVAI quartile, which was 93.263 (63.738, 114.807). Multivariate logistic regression analysis was used to predict the risk of cVAI on MAFLD, elevated ALT, and MS under different adjustment conditions. Then, the receiver operating characteristic (ROC) curves of the cVAI in different subgroups were plotted, and the area under the ROC curve (AUC), sensitivity, specificity, Youden index, and cutoff value were generated to evaluate the accuracy of the cVAI in predicting MAFLD, elevated ALT, and MS. The DeLong test was performed to examine the accuracy of the cVAI, WC, WHtR, and BMI in predicting MAFLD. We also constructed a novel prediction model for MAFLD using a binary logistic regression model and evaluated its efficacy. The effects of the cVAI on ALT, AST/ALT, and NFS were investigated using multiple linear regression analysis under different adjustment conditions.

A difference was considered to be statistically significant when $P < 0.05$. All the data were analysed by SPSS 26.0, GraphPad Prism 8, and MedCalc software.

Results

Characteristics of the Participants

Table 1 displays the demographic, anthropometric, and laboratory test data of 541 nonobese individuals. Age, and the percentage of hypertension, diabetes, smoking history, and drinking history were all greater in the MAFLD group than in the non-MAFLD group ($P < 0.05$). Participants in the MAFLD group had higher SBP, DBP, WC, BMI, WHtR, cVAI, ALT, AST, NFS, TC, TG, LDL-C, FBG, and SUA but had lower AST/ALT and HDL-C levels ($P < 0.05$). In addition, the

Table 1 Characteristics of Participants in the MAFLD Group and Non-MAFLD Group

Baseline data	MAFLD Group (n = 188)	Non-MAFLD Group (n = 353)	P-value *
Male / Female (n / n)	136/52	232/121	0.116
Age year [M (P_{25}, P_{75})]	41.00 (35.00, 52.25)	36.00 (30.00, 43.00)	< 0.001
Level of education			0.916
High school and below (n)	79	150	
University and above (n)	109	203	
Hypertension [n (%)]	64 (34.0%)	60 (17.0%)	< 0.001
Diabetes [n (%)]	19 (10.1%)	14 (4.0%)	0.004
Smoking history [n (%)]	62 (33.0%)	75 (21.2%)	0.003
Drinking history [n (%)]	54 (28.7%)	71 (20.1%)	0.024
SBP mmHg [M (P_{25}, P_{75})]	133.00 (122.00, 141.00)	124.00 (115.00, 133.00)	< 0.001
DBP mmHg [M (P25, P75)]	81.00 (75.75, 90.00)	76.00 (69.00, 83.00)	< 0.001
WC cm [M (P25, P75)]	92.00 (89.00, 95.00)	86.00 (80.00, 91.00)	< 0.001
BMI kg/m^2 [M (P_{25}, P_{75})]	26.00 (24.84, 27.12)	24.28 (22.39, 25.95)	< 0.001
WHtR [M (P_{25}, P_{75})]	0.53 (0.52, 0.55)	0.50 (0.47, 0.53)	< 0.001
cVAI [M (P25, P75)]	114.81 (100.48, 129.50)	76.17 (48.70, 99.57)	< 0.001
ALT U/L [M (P_{25}, P_{75})]	31.00 (22.75, 42.00)	22.00 (15.00, 31.00)	< 0.001
ALT > 40 U/L [n (%)]	52 (27.7%)	45 (12.7%)	< 0.001
AST U/L [M (P_{25}, P_{75})]	22.00 (19.00, 26.00)	19.00 (17.00, 23.00)	< 0.001
AST > 40 U/L [n (%)]	7 (3.7%)	9 (2.5%)	0.443
AST/ALT [M (P_{25}, P_{75})]	0.71 (0.58, 0.85)	0.89 (0.71, 1.14)	< 0.001
NFS [M (P_{25}, P_{75})]	−3.13 (−4.03, −2.31)	−3.40 (−3.94, −2.79)	0.027
TC mmol/L $(\bar{x} \pm SD)$	4.84 ± 0.88	4.55 ± 0.81	< 0.001
TC ≥ 5.18 mmol/L [n (%)]	66 (35.1%)	74 (21.0%)	< 0.001
TG mmol/L [M (P_{25}, P_{75})]	2.06 (1.49, 2.83)	1.03 (0.73, 1.38)	< 0.001
TG ≥ 1.70 mmol/L [n (%)]	124 (66.0%)	41 (11.6%)	< 0.001
HDL-C mmol/L [M (P_{25}, P_{75})]	1.15 (1.00, 1.35)	1.32 (1.17, 1.52)	< 0.001
HDL-C < 1.04 mmol/L [n (%)]	54 (28.7%)	31 (8.8%)	< 0.001
LDL-C mmol/L $(\bar{x} \pm SD)$	2.95 ± 0.74	2.66 ± 0.70	< 0.001
LDL-C ≥ 3.37 mmol/L [n (%)]	55 (29.3%)	51 (14.4%)	< 0.001
FBG mmol/L [M (P_{25}, P_{75})]	5.56 (5.10, 5.89)	5.130 (4.90, 5.37)	< 0.001
FBG ≥ 6.10 mmol/L [n (%)]	34 (18.1%)	19 (5.4%)	< 0.001
SUA μmol/L $(\bar{x} \pm SD)$	365.96 ± 80.54	330.62 ± 84.44	< 0.001
Hyperuricaemia [n (%)]	57 (30.3%)	58 (16.4%)	< 0.001
Platelet ×10^9/L $(\bar{x} \pm SD)$	257.99 ± 63.00	251.08 ± 57.42	0.198
MS [n (%)]	92 (48.9%)	21 (5.9%)	< 0.001

Notes: *For comparisons between two groups, the *t* test was used when the quantitative data conformed to a normal distribution, the Wilcoxon rank sum test was used when the quantitative data conformed to a nonnormal distribution, and the χ^2 test was used for qualitative data.

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; WHtR, waist-height ratio; cVAI, Chinese Visceral Adiposity Index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NFS, NAFLD fibrosis score; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; SUA, serum uric acid; MS, metabolic syndrome.

percentages of MAFLD patients with elevated ALT, elevated TC, elevated TG, decreased HDL-C, elevated LDL-C, elevated FBG, hyperuricemia, and MS were strongly greater than those of non-MAFLD patients ($P < 0.001$).

Correlations Between the cVAI and MAFLD-Related Indicators

As illustrated in Figure 2, we further explored the correlations between the cVAI and MAFLD-related indicators. We detected weak correlations between cVAI and AST ($r = 0.30$), LDL-C ($r = 0.26$), and FBG ($r = 0.38$) and moderate correlations between cVAI and ALT ($r = 0.46$), AST/ALT ($r = -0.45$), TG ($r = 0.64$), HDL-C ($r = -0.44$), and SUA ($r = 0.41$).

Multivariate Logistic Regression Analysis of the cVAI for MAFLD in Nonobese Subjects

To further explore whether a higher cVAI has an impact on MAFLD in nonobese Chinese individuals, multivariate logistic regression analysis was performed. The patients were divided into quartiles according to the following criteria: cVAI 1 (< 63.738), cVAI 2 (63.738–93.263), cVAI 3 (93.263–114.807), and cVAI 4 (> 114.807).

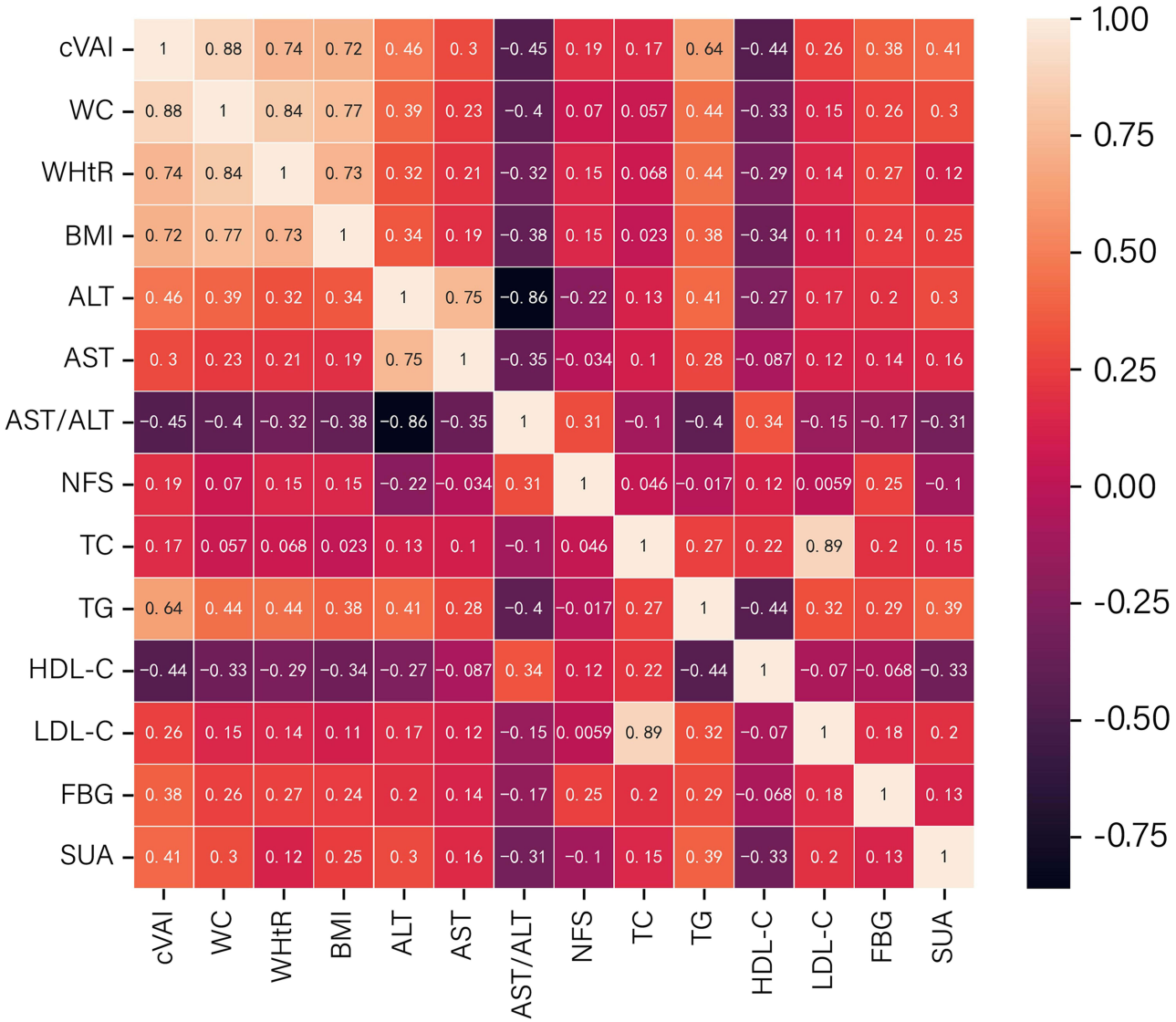


Figure 2 Heatmap of the correlation analysis between predictors and biochemical indicators.

Abbreviations: cVAI, Chinese Visceral Adiposity Index; WC, waist circumference; WHtR, waist-height ratio; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NFS, NAFLD fibrosis score; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; SUA, serum uric acid.

As shown in Figure 3A, higher cVAI quartiles were strongly associated with MAFLD in nonobese subjects. Compared to those of the cVAI 1 group, the ORs were [11.514 (95% CI: 3.407–38.909), $P < 0.001$], [37.370 (95% CI: 11.330–123.254), $P < 0.001$], and [101.951 (95% CI: 30.660–339.014), $P < 0.001$] for the cVAI 2, cVAI 3, and cVAI 4 groups, respectively, without adjustment (Model 1). After adjusting for age, smoking history and drinking history, the cVAI 2, cVAI 3, and cVAI 4 still had strong associations with MAFLD, with ORs of [11.096 (95% CI: 3.266–37.698), $P < 0.001$], [34.710 (95% CI: 10.392–115.928), $P < 0.001$], and [94.472 (95% CI: 27.550–323.954), $P < 0.001$], respectively (Model 2). This correlation was still significant after adjusting for other confounding variables, such as age, smoking history, drinking history, SBP, DBP, ALT, AST, TC, TG, HDL-C, LDL-C, FBG, and SUA (Model 3). Compared with those in the cVAI 1 group, the cVAI 2, cVAI 3, and cVAI 4 groups had significantly greater risk of MAFLD, with ORs of [4.334 (95% CI: 1.197–15.684), $P = 0.025$], [8.923 (95% CI: 2.391–33.297), $P = 0.001$], and [16.173 (95% CI: 4.082–64.073), $P < 0.001$], respectively.

Additionally, we conducted a subgroup analysis according to sex and median age (38 years). As demonstrated in Figure 3B, even after adjusting for confounders, we found that a higher cVAI remained a risk factor for nonobese MAFLD in the male, female, elderly (age > 38 years), and young (age ≤ 38 years) subgroups ($P < 0.05$).

ROC Curve of the Ability of the cVAI to Predict MAFLD in Nonobese Subjects

To evaluate the prognostic value of the cVAI for MAFLD in nonobese Chinese individuals of different sexes and ages, the ROC curves for the cVAI, WC, WHtR, and BMI were plotted. Figures 4 and 5 and Table 2 display the outcomes. The AUC of the cVAI for MAFLD was 0.828 (95% CI: 0.794–0.862). In males, females, elderly individuals, and young individuals, the cVAI had a better ability to predict the risk of MAFLD than did WC, the WHtR, or BMI, with AUCs of 0.833 (95% CI: 0.793–0.873), 0.905 (95% CI: 0.861–0.948), 0.774 (95% CI: 0.717–0.830), and 0.853 (95% CI: 0.807–0.900), respectively (Figure 4A-D). We further compared the AUCs between the subgroups and found that the AUC of the cVAI for MAFLD was substantially greater in participants who were female, younger, and highly educated than in male ($P = 0.0180$), elderly individuals ($P = 0.0327$), or less educated participants ($P = 0.0286$) (Figure 5A-D).

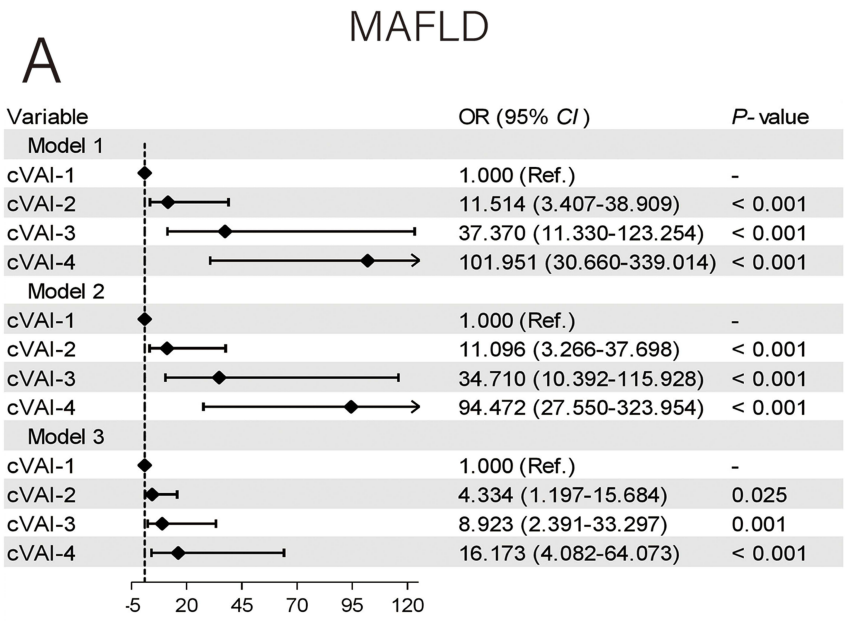
Establishment and Evaluation of the CWTS Model for Better Predicting MAFLD

To further improve the predictive ability of MAFLD, we constructed a new predictive model using the forward conditional method by putting the indicators with between-group differences into the binary logistic regression model. This model, which we abbreviate as CWTS, is constructed from the indicators cVAI, WHtR, TG, and SBP and is used to more accurately predict MAFLD. The regression equation for this model was: $-14.307 + 0.024 \times$ cVAI $+ 13.735 \times$ WHtR $+ 1.122 \times$ TG (mmol/L) $+ 0.019 \times$ SBP (mmHg) (Supplementary Table 1).

As shown in Table 3 and Figure 6, the AUC of the CWTS model for MAFLD was 0.883 (95% CI: 0.855–0.911), and the AUC of the CWTS model was greater for females, young individuals, and highly educated individuals than for males [0.915 (0.874–0.955) vs 0.880 (0.847–0.914), $P = 0.2000$], elderly individuals [0.908 (0.872–0.944) vs 0.837 (0.789–0.884), $P = 0.0193$], and less educated participants [0.905 (0.873–0.937) vs 0.859 (0.811–0.907), $P = 0.1156$] (Figure 6A-D). In addition, the AUC of the CWTS model for MAFLD was significantly greater than the AUC of the cVAI for MAFLD [0.883 (0.855–0.911) vs 0.828 (0.794–0.862), $P < 0.001$].

Multivariate Logistic Regression Analysis of cVAI for Elevated ALT in Nonobese Subjects

As shown in Figure 7A, higher cVAI quartiles were strongly associated with elevated ALT levels. Compared to those of the cVAI 1 group, the ORs were [2.442 (95% CI: 1.023–5.829), $P = 0.044$], [5.556 (95% CI: 2.468–12.509), $P < 0.001$], and [5.715 (95% CI: 2.543–12.842), $P < 0.001$] for the cVAI 2, cVAI 3, and cVAI 4 groups, respectively, in Model 1. In Model 2, the cVAI 2, cVAI 3, and cVAI 4 still had strong associations with elevated ALT levels, with ORs of [2.971 (95% CI: 1.230–7.175), $P = 0.016$], [7.607 (95% CI: 3.279–17.647), $P < 0.001$], and [8.611 (95% CI: 3.602–20.584), $P < 0.001$], respectively. This correlation remained significant after we adjusted for age, smoking history, drinking history, SBP, DBP, TC, TG, HDL-C, LDL-C, FBG, and SUA (Model 3*). Compared with those in the cVAI 1 group, the cVAI 2,



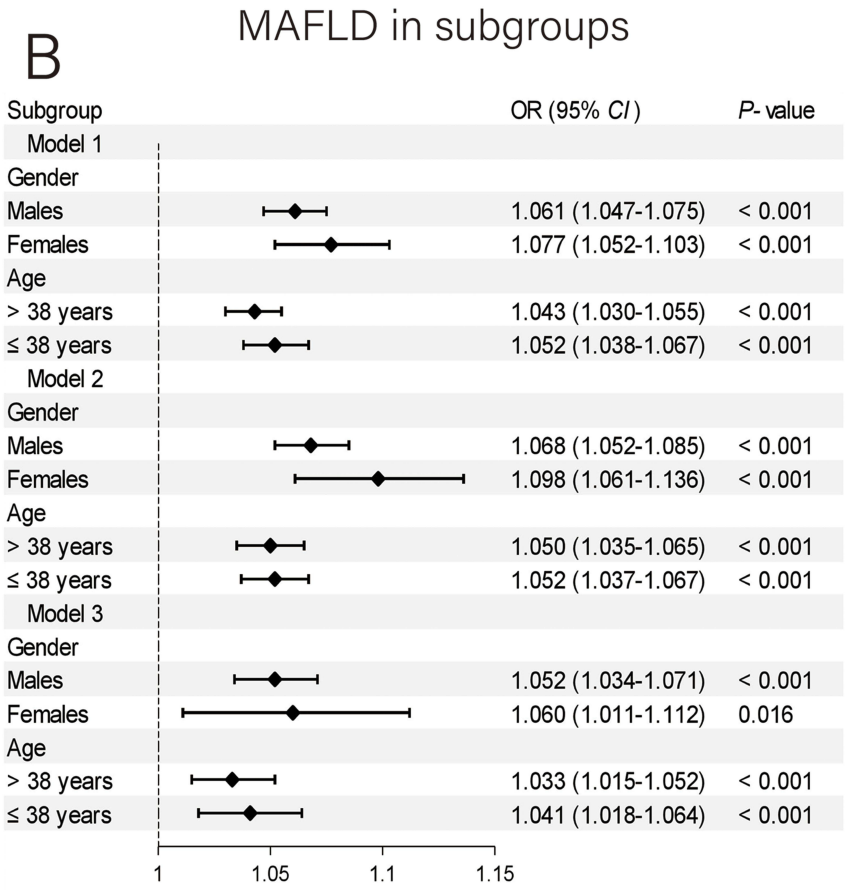


Figure 3 Logistic regression analysis of cVAI for MAFLD in nonobese subjects. (**A**) Logistic regression analysis of cVAI in predicting MAFLD; (**B**) Logistic regression analysis of cVAI in predicting MAFLD in different subgroups. Model 1: without adjustment; Model 2: adjusted for age, smoking history, and drinking history; Model 3: adjusted for age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, total serum cholesterol, serum triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, and serum uric acid.
Abbreviations: cVAI, Chinese Visceral Adiposity Index; MAFLD, metabolic dysfunction-associated fatty liver disease.

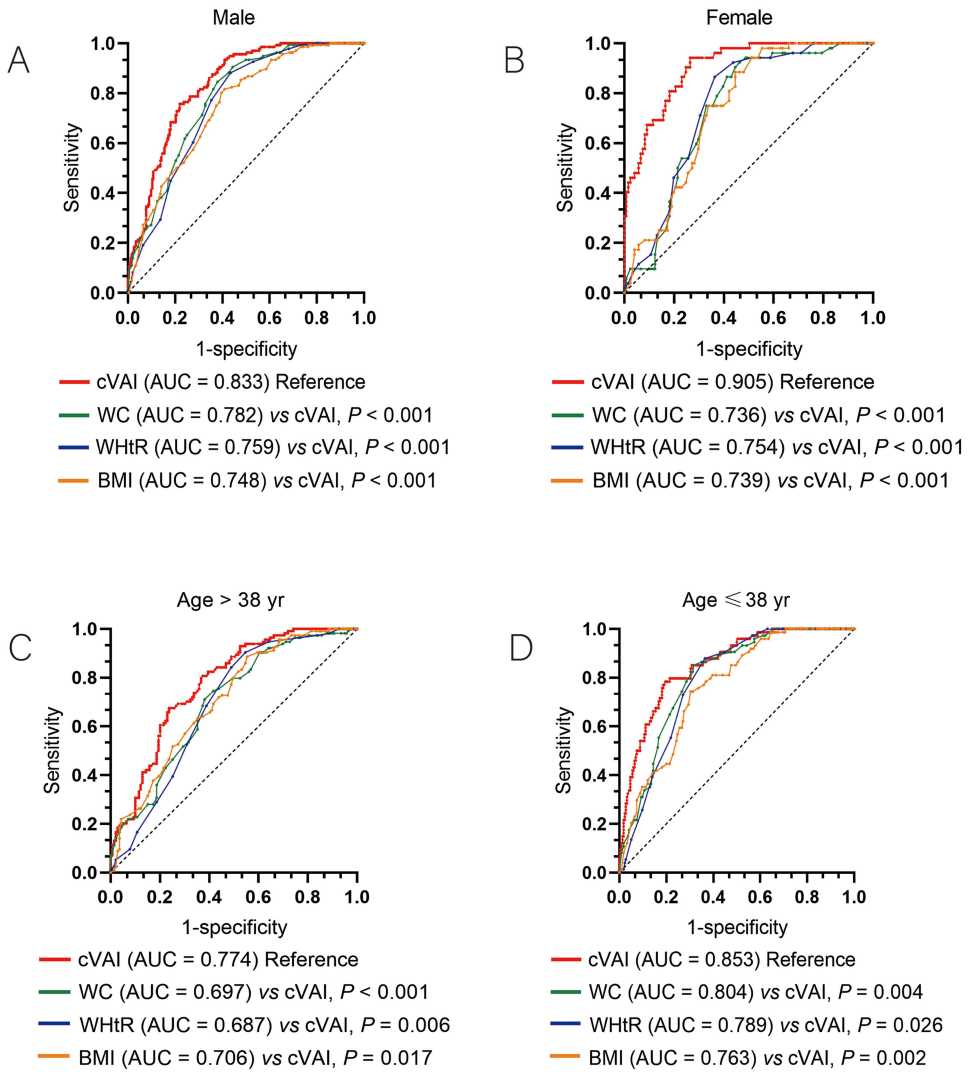


Figure 4 ROC curve of different indicators for predicting nonobese MAFLD in different subgroups. (**A**) Male subjects; (**B**) Female subjects; (**C**) Elderly (age > 38 years) subjects; (**D**) Young (age ≤ 38 years) subjects.

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index; WC, waist circumference; WHtR, waist-to-height ratio; BMI, body mass index.

cVAI 3, and cVAI 4 groups had significantly greater risk of elevated ALT, with ORs of [3.282 (95% CI: 1.265–8.512), $P = 0.015$], [7.741 (95% CI: 2.900–20.664), $P < 0.001$], and [8.463 (95% CI: 2.859–25.049), $P < 0.001$].

In addition, as demonstrated in Figure 7B, even after adjusting for confounders, a higher cVAI continued to be a risk indicator for elevated ALT in males, females, and young individuals ($P < 0.05$). In the subgroup of elderly individuals, the cVAI was also associated with the risk of elevated ALT in Models 1 and 2, but there was no correlation in Model 3* ($P = 0.051$).

ROC Curve of the cVAI for Predicting Elevated ALT Levels in Nonobese Subjects

To predict elevated ALT levels across subgroups according to sex, age, and educational qualification, ROC curves for the cVAI were generated, and the AUCs were compared between the subgroups. The AUC of cVAI for elevated ALT was 0.655 (95% CI: 0.602–0.708), and the AUC of cVAI were markedly greater in females, young, and highly educated compared to males [0.736 (0.625–0.847) vs 0.576 (0.511–0.641), $P = 0.0165$], elderly [0.737 (0.673–0.802) vs 0.599 (0.507–0.692), $P = 0.0173$], and less educated participants [0.704 (0.633–0.774) vs 0.582 (0.500–0.664), $P = 0.0277$]. Table 4 and Figure 8A-D display the outcomes.

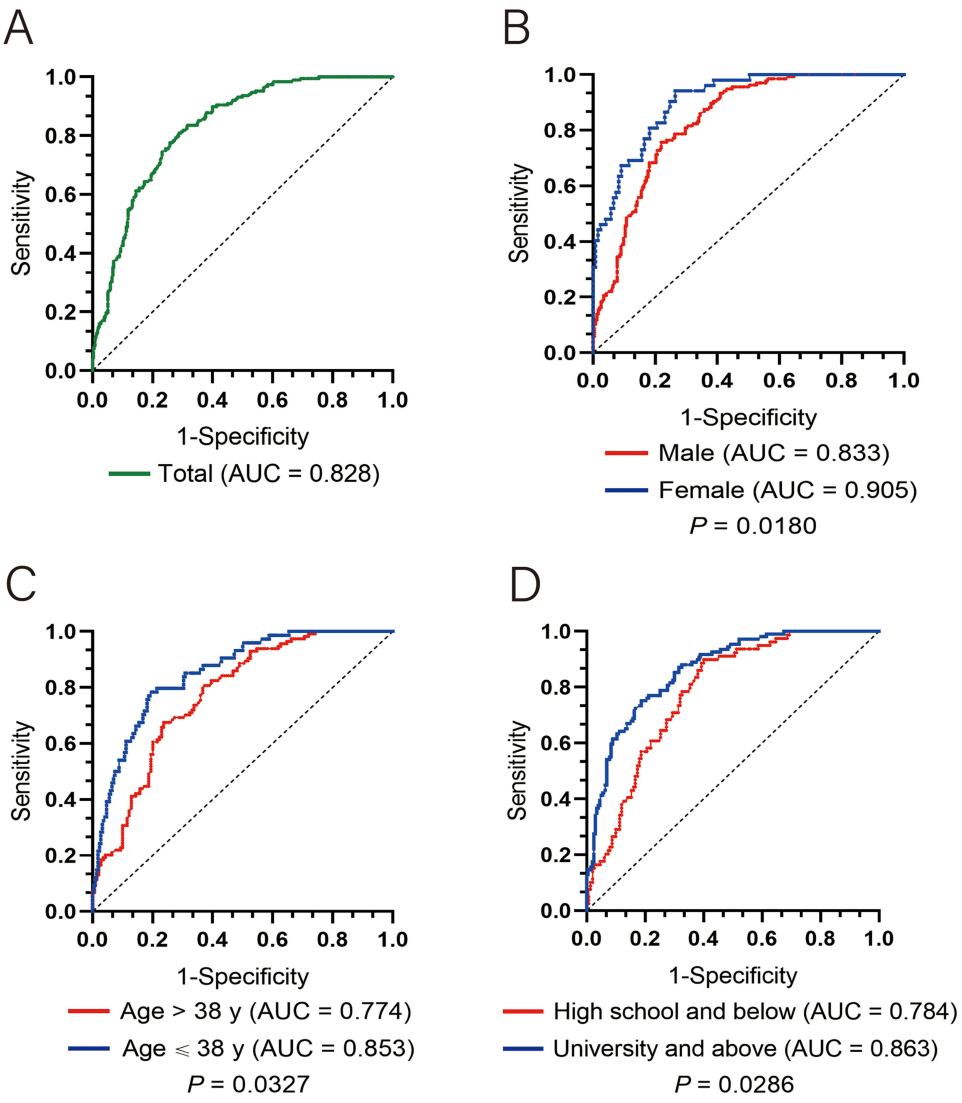


Figure 5 ROC curve of the ability of the cVAI to predict MAFLD in different subgroups of nonobese subjects. (**A**) Total subjects; (**B**) Comparison between male and female subjects (P = 0.0180); (**C**) Comparison between elderly (age > 38 years) and young (age ≤ 38 years) subjects (P = 0.0327); (**D**) Comparison between high school and university subjects (P = 0.0286).

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index.

Multiple Linear Regression Analysis of the Effect of the cVAI on MAFLD-Related Indicators in Nonobese Subjects

As shown in Table 5, ALT, AST/ALT, and NFS were strongly linked with the cVAI. The effects of various cVAIs on ALT levels, the AST/ALT ratio, and the NFS in Model 1 were significantly different ($P < 0.001$). In Model 2 or 2$^{\#}$ (adjusted for smoking history and drinking history), the cVAI still had strong associations with ALT, AST/ALT, and the NFS ($P < 0.001$). Additionally, there were still significant differences in the association between different cVAI values and ALT levels, AST/ALT, and NFS ($P < 0.001$) in Model 3* and Model 3$^{\#}$ (adjusted for smoking history, drinking history, SBP, DBP, TC, TG, HDL-C, LDL-C, and SUA).

Table 2 ROC Analysis of Different Indicators for Predicting Nonobese MAFLD in Different Subgroups

Indicators	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden Index	Cut-off value
Males					
cVAI	0.833 (0.793–0.873)	75.700	78.000	0.537	108.559
WC (cm)	0.782 (0.736–0.827) [a]	84.600	62.100	0.467	89.250
WHtR	0.759 (0.711–0.807) [a]	81.600	64.200	0.458	0.513
BMI (kg/m^2)	0.748 (0.699–0.798) [a]	80.100	61.200	0.413	25.213
Females					
cVAI	0.905 (0.861–0.948) [b]	94.200	73.600	0.678	65.382
WC (cm)	0.736 (0.662–0.810) [a]	92.300	53.700	0.460	81.250
WHtR	0.754 (0.682–0.825) [a]	86.500	63.600	0.501	0.514
BMI (kg/m^2)	0.739 (0.667–0.811) [a]	94.200	51.200	0.454	23.123
> 38 years					
cVAI	0.774 (0.717–0.830)	67.500	76.300	0.438	107.429
WC (cm)	0.697 (0.633–0.761) [a]	71.100	61.900	0.330	89.250
WHtR	0.687 (0.622–0.753) [a]	82.500	54.700	0.372	0.518
BMI (kg/m^2)	0.706 (0.643–0.769) [a]	88.600	44.600	0.332	24.251
≤ 38 years					
cVAI	0.853 (0.807–0.900) [c]	78.400	80.400	0.588	95.046
WC (cm)	0.804 (0.753–0.855) [a]	85.100	68.200	0.533	88.250
WHtR	0.789 (0.738–0.841) [a]	79.700	72.400	0.521	0.513
BMI (kg/m^2)	0.763 (0.706–0.819) [a]	74.300	69.600	0.439	25.148

Notes: [a]represents $P < 0.05$ compared with the cVAI; [b] represents $P < 0.05$ compared with males; [c] represents $P < 0.05$ compared with age > 38 years.

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index; WC, waist circumference; WHtR, waist-to-height ratio; BMI, body mass index.

Table 3 ROC Analysis of the CWTS Model for Predicting Nonobese MAFLD Patients in Different Subgroups

Subgroups	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden Index	Cut-off value
Total	0.883 (0.855–0.911)	89.900	72.200	0.621	−0.956
Gender					
Males	0.880 (0.847–0.914)	91.900	69.800	0.617	−0.657
Females	0.915 (0.874–0.955)	76.900	89.300	0.662	−0.982
Age					
> 38 years	0.837 (0.789–0.884)	83.300	68.300	0.516	−0.486
≤ 38 years	0.908 (0.872–0.944)[a]	87.800	81.300	0.691	−0.961
Level of education					
High school and below	0.859 (0.811–0.907)	92.400	64.700	0.571	−0.956
University and above	0.905 (0.873–0.937)	88.100	78.300	0.664	−0.910

Notes: [a] represents $P < 0.05$ compared with age > 38 years.

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; CWTS, prediction model combining the Chinese Visceral Adiposity Index, waist-to-height ratio, triglyceride, and systolic blood pressure.

Multivariate Logistic Regression Analysis of the cVAI for MS in Nonobese MAFLD Patients

As shown in Figure 9, higher cVAI quartiles were strongly associated with MS in nonobese MAFLD patients. Compared to those in the cVAI 1 group, the ORs were [3.798 (95% CI: 1.610–8.959), $P = 0.002$] and [5.029 (95% CI: 2.095–12.072), $P < 0.001$] for the cVAI 3 and cVAI 4 groups, respectively, in Model 1. According to Model 2, the cVAI 3 and cVAI 4 groups still exhibited strong associations with MS, with ORs of [4.547 (95% CI: 1.852–11.167), $P = 0.001$] and [6.675 (95% CI: 2.504–17.796), $P < 0.001$], respectively. Additionally, compared with those in the cVAI 1 group, the risk

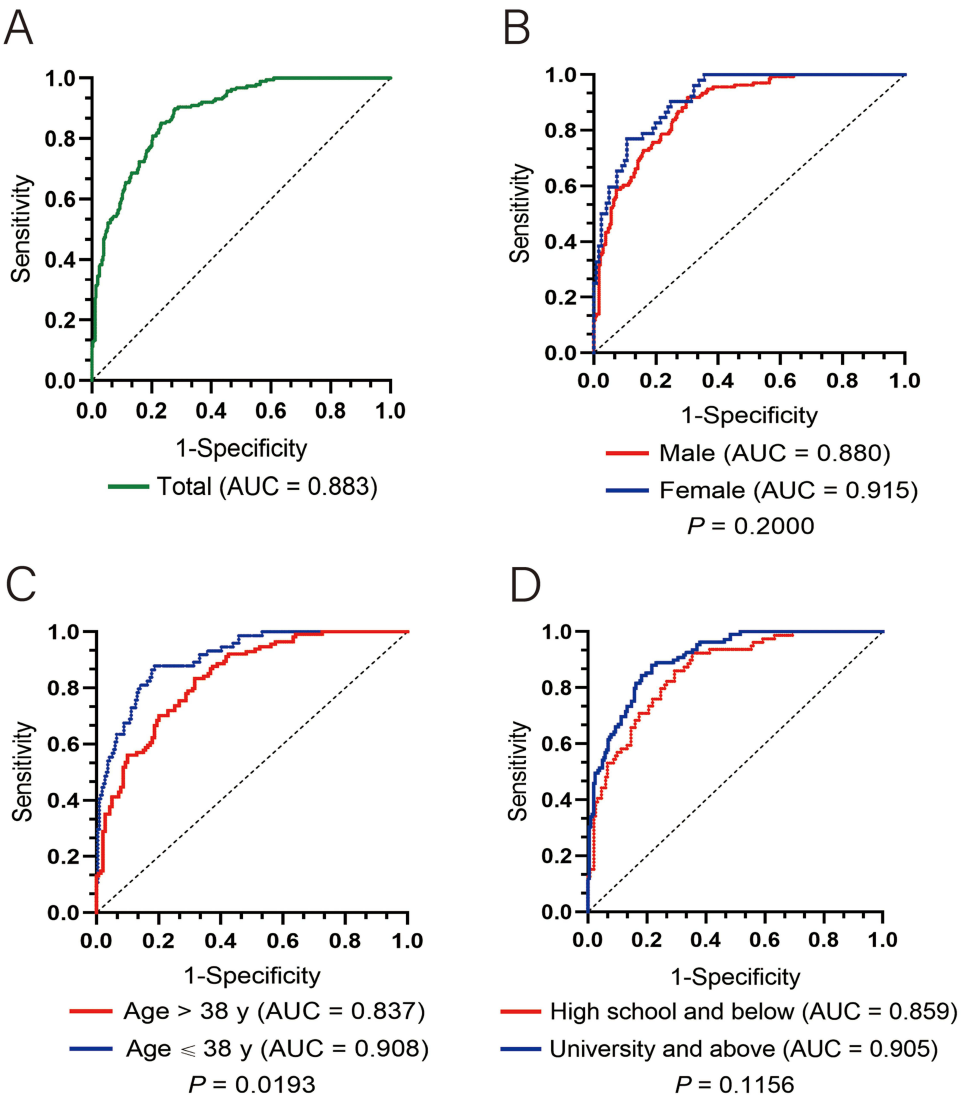


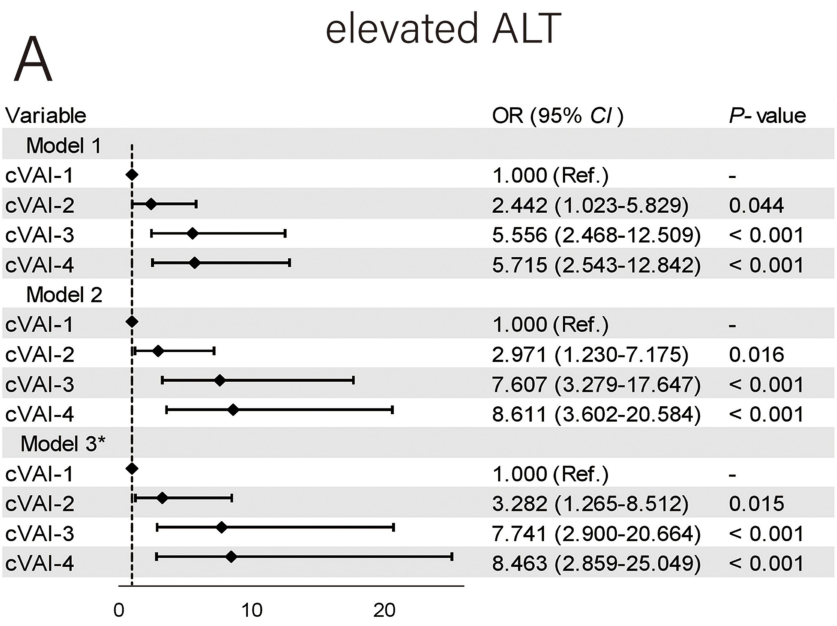
Figure 6 ROC curve of the CWTS model for predicting MAFLD in different subgroups of nonobese subjects. (**A**) Total subjects; (**B**) Comparison between male and female subjects (P = 0.2000); (**C**) Comparison between elderly (age > 38 years) and young (age ≤ 38 years) subjects (P = 0.0193); (**D**) Comparison between high school and university subjects (P = 0.1156).

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; CWTS, prediction model combining the Chinese Visceral Adiposity Index, waist-to-height ratio, triglyceride, and systolic blood pressure.

of MS was markedly greater in the cVAI 3 and cVAI 4 groups according to Model 3, with ORs of [5.406 (95% CI: 1.786–16.362), P = 0.003] and [6.328 (95% CI: 1.742–22.992), P = 0.005], respectively.

ROC Curve of the cVAI for Predicting MS in Nonobese MAFLD Patients

The ROC curves were plotted for the ability of the cVAI to predict MS across sex, age, and education qualification subgroup, and the AUCs were compared between the subgroups. The AUC of the cVAI for MS was 0.688 (95% CI: 0.612–0.763). The AUC of the cVAI was greater for males, elderly individuals, and less educated individuals than for females [0.747 (0.665–0.828) vs 0.660 (0.511–0.808), P = 0.3173], young individuals [0.732 (0.641–0.824) vs 0.604 (0.471–0.737), P = 0.1233], and highly educated participants [0.767 (0.663–0.871) vs 0.636 (0.532–0.740), P = 0.0815], although no substantial difference was observed. Figure 10A-D and Table 6 show the results.



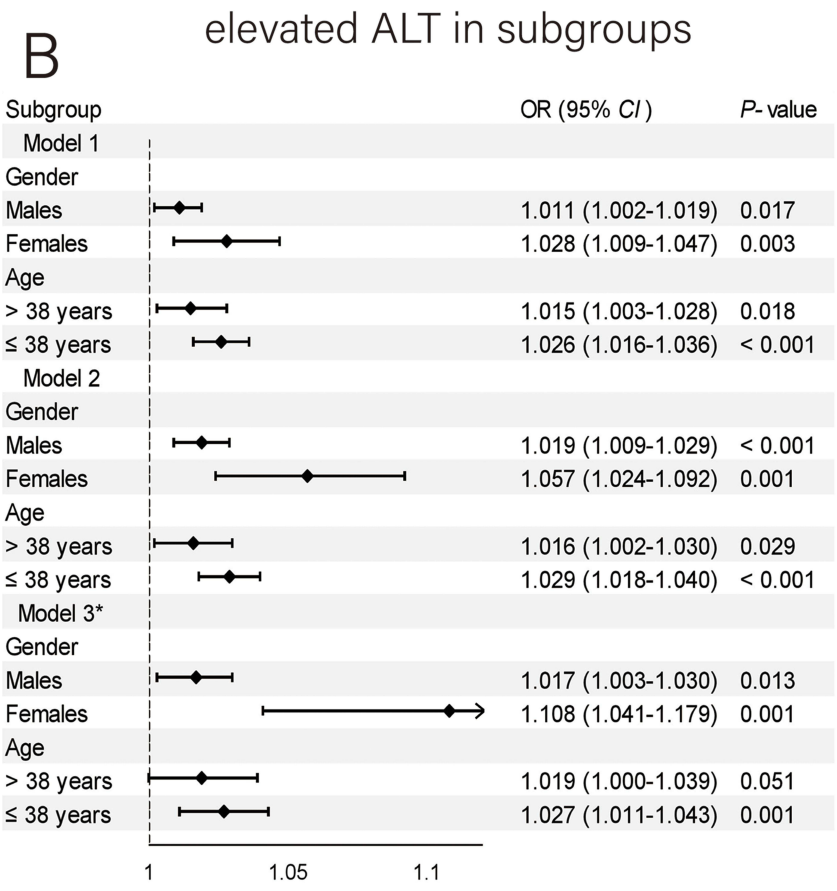


Figure 7 Logistic regression analysis of cVAI for elevated ALT in nonobese subjects. (**A**) Logistic regression analysis of cVAI in predicting elevated ALT; (**B**) Logistic regression analysis of cVAI in predicting elevated ALT in different subgroups. Model 1: without adjustment; Model 2: adjusted for age, smoking history, and drinking history; Model 3*: adjusted for age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, total serum cholesterol, serum triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, and serum uric acid.

Abbreviations: cVAI, Chinese Visceral Adiposity Index; ALT, alanine aminotransferase.

Table 4 ROC Analysis of the Ability of the cVAI to Predict Elevated ALT Levels in Different Subgroups of Nonobese Subjects

Subgroups	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden Index	Cut-off value
Total	0.655 (0.602–0.708)	75.300	53.800	0.291	91.181
Gender					
Males	0.576 (0.511–0.641)	79.300	41.300	0.206	94.349
Females	0.736 (0.625–0.847) [a]	80.000	67.700	0.477	73.854
Age					
> 38 years	0.599 (0.507–0.692)	94.900	25.700	0.206	79.918
≤ 38 years	0.737 (0.673–0.802) [b]	74.100	68.300	0.424	90.211
Level of education					
High school and below	0.582 (0.500–0.664)	75.500	46.700	0.222	93.171
University and above	0.704 (0.633–0.774) [c]	79.200	57.200	0.364	88.889

Notes: [a]represents $P < 0.05$ compared with males; [b]Represents $P < 0.05$ compared with age > 38 years; [c] represents $P < 0.05$ compared with education of high school and below.

Abbreviations: ALT, alanine aminotransferase; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index.

Discussion

In the present research, the associations between cVAI and MAFLD and elevated ALT in nonobese Chinese individuals were thoroughly examined, and the prognostic significance of the cVAI for MAFLD and elevated ALT was evaluated.

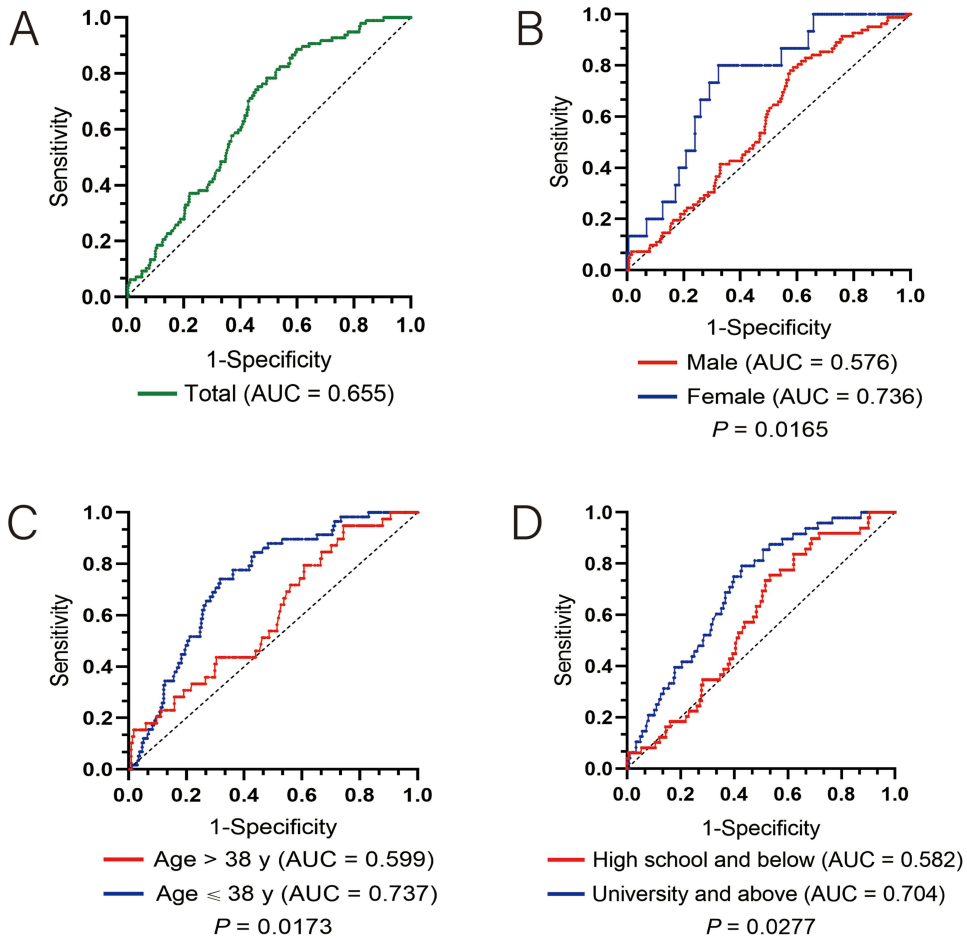


Figure 8 ROC curve of the ability of the cVAI to predict elevated ALT levels in different subgroups of nonobese subjects. (**A**) Total subjects; (**B**) Comparison between male and female subjects ($P = 0.0165$); (**C**) Comparison between elderly (age > 38 years) and young (age ≤ 38 years) subjects ($P = 0.0173$); (**D**) Comparison between high school and university subjects ($P = 0.0277$).

Abbreviations: ALT, alanine aminotransferase; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index.

Table 5 Multiple Linear Regression Analyses of the Effect of the cVAI on MAFLD-Related Indicators

Variable	Model	B	S.E.	Standardized value β	t	*P*-value
ALT	Model 1	0.185	0.026	0.292	7.093	< 0.001
	Model 2	0.248	0.029	0.391	8.419	< 0.001
	Model 3 *	0.276	0.042	0.436	6.605	< 0.001
AST/ALT	Model 1	−0.004	< 0.001	−0.456	−11.911	< 0.001
	Model 2	−0.005	< 0.001	−0.558	−13.084	< 0.001
	Model 3 *	−0.005	0.001	−0.491	−8.099	< 0.001
NFS	Model 1	0.007	0.001	0.227	4.823	< 0.001
	Model 2 #	0.007	0.001	0.236	4.830	< 0.001
	Model 3 #	0.015	0.002	0.498	8.055	< 0.001

Notes: Model 1: without adjustment; Model 2: adjusted for age, smoking history, and drinking history; Model 2 #: adjusted for smoking history and drinking history; Model 3 *: adjusted for age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, total serum cholesterol, serum triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, and serum uric acid; Model 3#: adjusted for smoking history, drinking history, systolic blood pressure, diastolic blood pressure, total serum cholesterol, serum triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and serum uric acid.
Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; cVAI, Chinese Visceral Adiposity Index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NFS, NAFLD fibrosis score.

The results suggested that the cVAI demonstrated excellent ability to predict MAFLD and elevated ALT in nonobese subjects. The effectiveness of the CWTS model constructed from the cVAI in conjunction with the WHtR, TG, and SBP for predicting MAFLD and its subgroups was also significant. This study also preliminarily explored the association between the cVAI and the NFS, and revealed that a greater cVAI was associated with a greater degree of hepatic fibrosis. Additionally, the cVAI also had certain predictive value for MS in patients with MAFLD, which further broadened the application of the cVAI. These findings suggested that the cVAI, an obesity indicator, may be a valuable and promising biomarker for predicting the occurrence and progression of MAFLD in nonobese Chinese individuals.

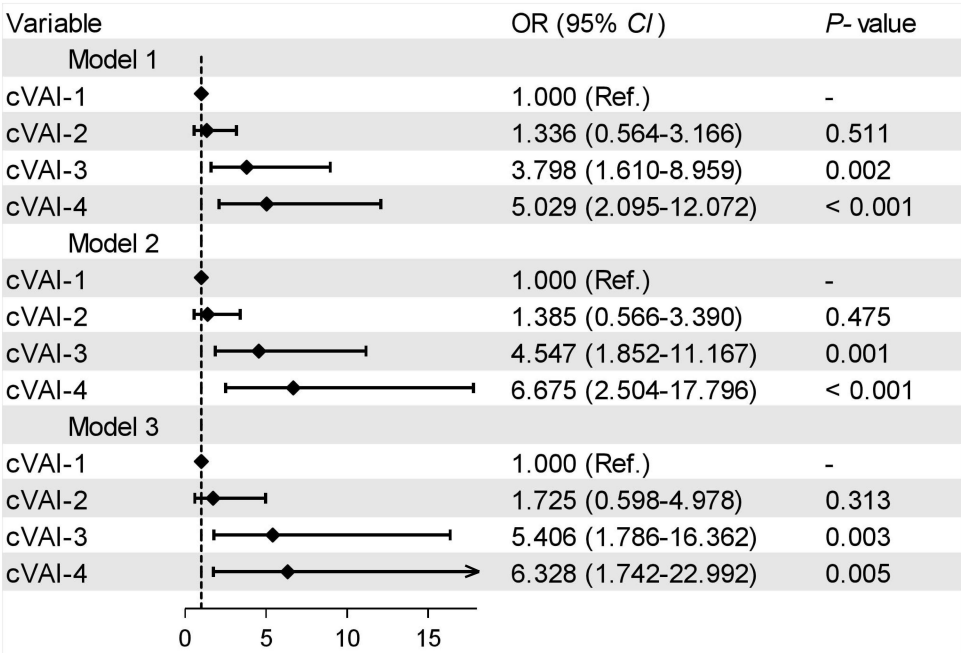


Figure 9 Logistic regression analysis of the ability of the cVAI to predict MS among nonobese MAFLD patients. Model 1: without adjustment; Model 2: adjusted for age, smoking history, and drinking history; Model 3: adjusted for age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, serum total cholesterol, serum triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, and serum uric acid.

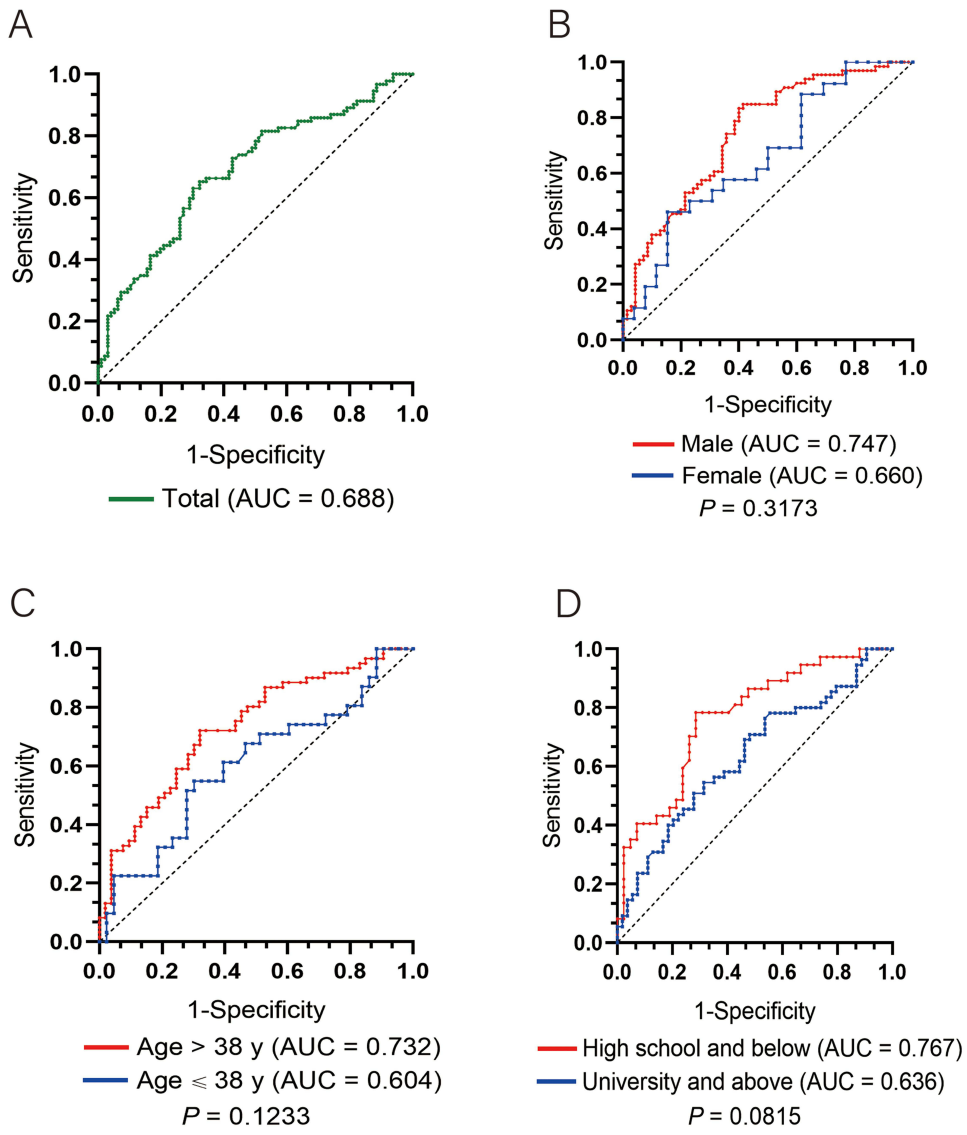


Figure 10 ROC curve of the cVAI for predicting MS in different subgroups of nonobese MAFLD patients. (**A**) Total subjects; (**B**) Comparison between male and female subjects (P = 0.3173); (**C**) Comparison between elderly (age > 38 years) and young (age ≤ 38 years) subjects (P = 0.1233); (**D**) Comparison between high school and university subjects (P = 0.0815).

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; MS, metabolic syndrome; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index.

There is a review that stated that nonobese MAFLD is common and that the prognosis for this group of patients may be similar to that of obese patients with MAFLD and worse than those without MAFLD.[12] Although the underlying pathophysiologic mechanisms of nonobese MAFLD are unclear, metabolic dysregulation may be considered a key determinant.[12,15] And the mechanisms that influence metabolic health include genetics, diet, physical activity, and gut microbiota.[15] Metabolic flexibility played an important role in shaping metabolic health, which referred to the ability of the human body to adapt to metabolic or energy demands by elaborating dynamic responses in the cellular machinery.[33] Smith and Kahn et al[34] suggested that physiological indicators of metabolic abnormalities should include an accurate assessment of intrahepatic fat accumulation so that metabolic dysfunction could be recognized at an early stage. Furthermore, no specific guidelines exist for the management of nonobese MAFLD patients, but lifestyle interventions remain the cornerstone of treatment.[12] That is why it is important to screen nonobese MAFLD patients early by the convenient and cost-effective indicator.

Table 6 ROC Analysis of the Ability of the cVAI to Predict MS in Different Subgroups of Nonobese MAFLD Patients

Subgroups	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden index	Cut-off value
Total	0.688 (0.612–0.763)	65.200	67.700	0.329	115.722
Gender					
Males	0.747 (0.665–0.828)	84.800	58.600	0.434	115.793
Females	0.660 (0.511–0.808)	46.200	84.600	0.308	104.350
Age					
> 38 years	0.732 (0.641–0.824)	72.100	67.900	0.400	114.807
≤ 38 years	0.604 (0.471–0.737)	54.800	69.800	0.246	116.895
Level of education					
High school and below	0.767 (0.663–0.871)	78.400	71.400	0.498	115.328
University and above	0.636 (0.532–0.740)	50.900	72.200	0.231	119.892

Abbreviations: MAFLD, metabolic dysfunction-associated fatty liver disease; MS, metabolic syndrome; ROC, receiver operating characteristic curve; AUC, area under the ROC curve; cVAI, Chinese Visceral Adiposity Index.

Recently, adipose tissue dysfunction was shown to play a significant role in the pathophysiology of fatty liver disease.[35] Kershaw et al[36] showed that white adipose tissue could secrete adipokines and various inflammatory factors, which participate in lipid metabolism and inflammatory responses. In turn, these factors enhance the fat-breaking activity of lipid cells and reduce their sensitivity to insulin, which is considered to be the mechanism for the pathogenesis of MAFLD.[37] Furthermore, nonobese MAFLD patients could have excess visceral adipose tissue,[38] which is especially related to insulin resistance, metabolic unhealthy obesity, and hepatic steatosis.[39,40] Increased free fatty acids (FFAs) are produced in the liver, where they act as ligands for toll-like receptors and induce cytokine production, thereby promoting inflammatory pathways associated with MAFLD.[41] Increased FFAs in the liver also increase dyslipidemia and hepatic fat deposition.[42]

The cVAI was derived from a multivariate linear regression analysis of 485 subjects who underwent abdominal computed tomography to examine the visceral adipose area and was verified again in 6495 participants enrolled in another area.[18] According to several studies, in the Chinese population, the cVAI may be a dependable and useful index for measuring visceral adipose functional dysfunction.[18,43] Previous studies[18,44] concluded that the cVAI was more valuable than BMI and WC in evaluating metabolic risks such as hypertension, diabetes and prediabetes. In addition to being associated with metabolism-related diseases,[19–21] cVAI was also closely related to the new occurrence of heart attack and renal damage in Chinese hypertensive patients.[45]

There are several possible explanations for the ability of the cVAI to predict MAFLD. Age, BMI, WC, TG, and HDL-C have been reported to be significantly associated with the risk of MAFLD,[46–48] and similar results were obtained in this study. Accumulating evidence suggests that abnormalities in hepatic and extrahepatic fat metabolism are the major causative factors of MAFLD.[49] Hepatic lipid accumulation eventually triggers lipid peroxidative stress and hepatic injury.[50] Therefore, understanding why the cVAI calculated from these five indicators could serve as a predictive marker for MAFLD is not difficult. Moreover, this study revealed that the cVAI had considerably better predictive accuracy for nonobese MAFLD than did WC, the WHtR, or BMI according to different subgroup analyses, which further highlighted the reliability of the cVAI.

Compared to the findings of other studies, the present study also explored the predictive value of the cVAI for elevated ALT in a nonobese population. ALT and AST levels are commonly used to assess inflammation in the liver. Elevated ALT levels and a decreased AST/ALT ratio suggest the development of MAFLD and the presence of steatohepatitis, with a significantly increased risk of worsening liver fibrosis and cancer.[25] Visceral fat storage may increase oxidative stress and mild inflammation and predispose patients to hepatic injury.[51] Several studies have shown that ALT is an enzyme closely associated with visceral fat accumulation,[52,53] which might be associated with the increase in hepatotoxic fatty acids due to visceral fat deposition.[52] Additionally, older age, higher BMI, WC, TG, and lower HDL-

C are commonly related to poorer incidence of hepatic disease in MAFLD patients,[47,54] which may explain the good predictive efficacy of the cVAI for elevated ALT levels.

The prevalence of MAFLD varied among the different subgroups, so we performed subgroup analyses according to sex, age, and education. The cVAI had better predictive efficacy for nonobese MAFLD and elevated ALT in females and younger participants, which was consistent with our previous findings.[11,24] Males may be more likely to be affected by MAFLD due to unhealthy lifestyles and lack of exercise. In addition, higher levels of estrogen, which inhibits visceral adipose deposition, may also be responsible for the lower incidence of MAFLD in females.[7,11,55] Numerous reports have demonstrated that the incidence of MAFLD increases with age, which may be related to metabolism, coexisting diseases, and physical inactivity.[7,11,56] Hence, the predictive value of the cVAI may be affected by age and sex. Furthermore, we were surprised to find that the cVAI had better predictive efficacy in highly educated subjects, possibly due to a better standard of living and healthier dietary habits.[7] These results suggested that we could monitor and manage different populations of patients, providing innovative ideas and methods for preventing and treating MAFLD.

Considering the progression of MAFLD, we further examined the connection between the cVAI and hepatic fibrosis. Our study's preliminary findings showed that the cVAI was positively correlated with the NFS, which is a score of the degree of hepatic fibrosis.[32] Li et al[57] also reported that the cVAI showed excellent predictive value for diagnosing fibrosis. In addition, the progression of MAFLD is often closely associated with MS. MAFLD patients with MS have a greater chance of experiencing adverse events, such as cardiovascular disease, liver-related complications, and extrahepatic malignancies.[58] We also found that the cVAI had good predictive value for MS in patients with MAFLD, which further confirmed our conjecture. Therefore, we believe that the cVAI has an early warning effect on MAFLD combined with MS.

However, studies examining the association between the cVAI and fatty liver have been rare. According to Chen et al,[23] fatty liver and the cVAI were independently associated. A clinical study carried out by Tang et al[22] also demonstrated that the cVAI was positively correlated with MAFLD in T2DM patients. This research may complement prior research and demonstrated that the predictive ability of the cVAI was also applicable to nonobese MAFLD patients and patients with elevated ALT levels. Importantly, some nonobese MAFLD patients were more likely to develop comorbid metabolic diseases, cardiovascular disease, or death than obese MAFLD patients were.[38,59] In addition, we conducted stratified analyses according to sex, age, and educational qualification; these factors were not addressed in any of the other studies. The predictive efficacy of the cVAI was also compared with that of classic obesity indicators, and the cVAI was found to be superior to these indices in this research. We also constructed a prediction model consisting of the cVAI and other metabolism-related indicators that showed excellent predictive efficacy for MAFLD.

Ultrasound is an efficient and convenient method for diagnosing fatty liver, but ultrasound can only identify hepatocellular steatosis and cannot determine whether the disease is caused by metabolic dysfunction.[26] ALT is a quick and simple indicator to determine the inflammatory state of the liver, but it is only significantly elevated in patients with severe MAFLD. And a variety of etiologies of liver diseases could cause ALT elevated.[60] This reflects the poor sensitivity and specificity of ALT for diagnosing MAFLD. In addition, hepatic steatosis index (HSI) and fatty liver index (FLI) also have great efficacy in predicting fatty liver, but unfortunately this study did not compare cVAI with HSI and FLI. Lee et al[61] and Bedogni et al[62] found that the AUCs of HSI and FLI for diagnosis of fatty liver were 0.812 (95% CI: 0.801–0.824) and 0.84 (95% CI: 0.81–0.87), which were similar to that of cVAI in this study. However, there are no studies exploring the HSI and FLI for diagnosing nonobese MAFLD. Therefore, we believe that cVAI is a meaningful score for the diagnosis of nonobese MAFLD.

However, the research we conducted has several limitations. First, this cross-sectional study raises questions about the causal link between cVAI and the onset of MAFLD and elevated ALT. Second, the findings of this study might be influenced by the small sample size and single-center design. However, the population enrolled met the minimum sample size required for this study. These findings should be confirmed in multicenter, large sample size cohort studies in our future work. Finally, as the gold standard for diagnosis, liver biopsy was not used to diagnose fatty liver in this study, which is not applicable in most of the Chinese population. Liver biopsy is an invasive and expensive procedure and is not suitable for large-scale population screening. Recent studies have reported that in addition to histology, hepatic steatosis

could be demonstrated by liver ultrasound.[22,23,63] Therefore, we believe that ultrasound is also the currently accepted method of diagnosis.

Conclusion

Generally, a higher cVAI was independently linked favorably to nonobese MAFLD, elevated ALT, and MS risk. We believe that the cVAI could serve as a reliable and accessible marker for identifying MAFLD and elevated ALT in the nonobese Chinese population in clinical practice. This approach may help to screen nonobese MAFLD patients and their progression in advance and to intervene early and effectively to improve their outcome.

Data Sharing Statement

The datasets generated during and/or analysed during the current study are available from the corresponding author (Shukun Yao, E-mail: shukunyao@126.com) on reasonable request.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Clinical Research of China-Japan Friendship Hospital (Approval No.: 2018-110-K79-1).

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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Disclosure

Zuohu Niu, Jialiang Chen and Huijing Wang are co-first authors for this study. The authors report no conflicts of interest in this work.

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