ORIGINAL RESEARCH

Sex-Specific Contribution of Cardiometabolic Index in Predicting Metabolic Dysfunction-Associated Fatty Liver Disease: Insights from a General Population

Dongxing Gu[1,*], Yayun Lu [iD][1,*], Baiqing Xu[1], Xuefeng Tang[2]

[1]Health Examination Center, Huadong Sanatorium, Wuxi, People's Republic of China; [2]Department of Health Nursing, Huadong Sanatorium, Wuxi, People's Republic of China

*These authors contributed equally to this work

Correspondence: Baiqing Xu; Xuefeng Tang, Huadong Sanatorium, No. 67 Jinyuan Road, Wuxi, 214065, People's Republic of China, Email doctorxbq@163.com; 978665164@qq.com

Background and Objective: Evidence suggests that cardiometabolic index (CMI) has been identified as a novel obesity-related index associated with diabetes, hypertension, and cardiovascular disease. Current evidence suggests that the differences in sex hormones and regional fat distribution in both sexes are directly correlated with metabolic dysfunction-associated fatty liver disease (MAFLD) risk. This study aimed to investigate the diagnostic value of CMI in MAFLD in both sexes.
Methods: This retrospective study included 6107 subjects who underwent annual health check-ups from March 2021 to January 2022. CMI was calculated by multiplying the ratio of triglycerides and high-density lipoprotein cholesterol (TG/HDL-C) by waist-to-height ratio (WHtR). Multivariable logistic regression analysis and restricted cubic spline were used to investigate the association of CMI and MAFLD risk. Receiver operating characteristic curve analysis was conducted for the exploration of the diagnostic accuracies of obesity-related indicators. Areas under the curves (AUCs) with 95% CIs were calculated.
Results: Prevalence of MAFLD increased with elevated quartiles of CMI in both sexes. The median (IQR) age was 46.00 (18.00) years. Multivariate logistic regression analyses showed that higher CMI was independently associated with MAFLD, in which every additional standard deviation (SD) of CMI increased the risk of MAFLD (OR=2.72, 95% CI:2.35–3.15 for males; OR=3.26, 95% CI:2.36–4.51 for females). Subjects in the fourth quartile of CMI had the highest odds of MAFLD for males (OR=15.82, 95% CI:11.84–21.14) and females (OR=22.60, 95% CI:9.52–53.65)(all P for trend<0.001). Besides, CMI had a non-linearity association with MAFLD (all P for non-linearity<0.001). Furthermore, CMI exhibited the largest AUC compared to other obesity-related indexes in terms of discriminating MAFLD in males (AUC=0.796, 95% CI:0.782–0.810) and females (AUC=0.853, 95% CI:0.834–0.872).
Conclusion: CMI was a convenient indicator for the screening of MAFLD among Chinese adults. Females with high CMI had a better diagnostic value for MAFLD than males.
Keywords: metabolic dysfunction-associated fatty liver disease, cardiometabolic index, sex, general population, predicting value

Introduction

Recent research has proposed the term Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) to better reflect the current understanding of fatty liver disease associated with metabolic dysfunction.[1,2] MAFLD is a diagnosis that is based on the presence of hepatic steatosis and the coexistence of a set of metabolic risk factors.[3] This new term is thought to identify individuals who are at a higher risk of developing hepatic and extrahepatic complications than those with non-alcoholic fatty liver disease (NAFLD).[4–6] It is estimated that MAFLD affects a quarter of the world's adult population, creating a large burden for individuals, families, and healthcare systems.[7,8] Progression of MAFLD can lead to

steatohepatitis, cirrhosis, and hepatocellular carcinoma[9–11] as well as other metabolic dysfunctions such as insulin resistance, diabetes, dyslipidemia, chronic kidney disease, cardiovascular and cerebrovascular diseases.[12–15]

Diagnosis of hepatic steatosis is a challenge due to the limitations of the available methods. Liver biopsy is considered the "gold standard" but is not widely used due to its invasive nature, high cost, and poor patient compliance. Ultrasound is the most commonly used method, but its sensitivity for mild steatosis is low and can be affected by the equipment and operator. Computed tomography (CT) has good diagnostic sensitivity, but its use is limited by radiation exposure. Magnetic resonance imaging (MRI) is noninvasive, precise, and reproducible, but it is more expensive and has lower specificity.[8,16,17] Therefore, it is essential to identify and diagnose MAFLD simply and effectively to prevent and delay its progression and related complications.

It has been well-established that there is a link between dyslipidemia, obesity, and fatty liver disease.[18,19] The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio is regarded as a reliable predictor of the risk of nonalcoholic fatty liver disease (NAFLD), as it can indicate insulin resistance (IR) in those with NAFLD.[20–22] The waist-to-height ratio (WHtR) is a combination of waist circumference (WC) and height, and is considered to be more effective than traditional body measurements in identifying abdominal obesity, assessing MAFLD, and predicting cardiac metabolic risks and a range of other non-communicable diseases.[23–26] Wakabayashi et al developed a marker called cardiometabolic index (CMI), which is calculated as WHtR multiplied by TG/HDL-C ratio, and combines lipid and obesity parameters into one simple and repeatable marker for the effective identification of diabetes.[27,28] Studies have also shown that CMI is significantly associated with hypertension, stroke, cardiovascular disease, and kidney disease.[29–32] This suggests that CMI is a valuable indicator of metabolic diseases. Additionally, there is potential for a sex-specific difference in CMI action, as the prevalence of MAFLD and CMI can vary between sexes. It has been observed in previous studies that higher CMI in the general population is independently associated with a higher risk of NAFLD in health check-up populations.[33,34] Nevertheless, there is yet to be research done on the potential relationship between CMI and MAFLD risk.

Therefore, this research aimed to explore the correlation between CMI and MAFLD, and evaluate the predictive value of CMI for MAFLD in different genders, to give a theoretical foundation for the screening of MAFLD among a Chinese adult population.

Methods
Study Population
This retrospective study was conducted at the Health Examination Center of Huadong Sanatorium between March 2021 to January 2022. A total of 6733 participants were initially included, however, those with incomplete medical information, under the age of 18, or with a history of malignancy or liver surgery were excluded (Figure 1). Consequently, this study included 6107 participants, with 3851 males and 2256 females, ranging in age from 18 to 91 (the median age being 46.45 and IQR 18 years). Demographic data such as age, gender, and cigarette/alcohol use were collected. Smoking was defined as smoking three or more cigarettes daily in a year, and alcohol consumption was defined as at least three times a week for at least twelve months.

This retrospective study, conducted in accordance with the Declaration of Helsinki, was granted approval by the Health Examination Center of Huadong sanatorium Ethics and Research Committee (approval number. 2023–10). To protect the privacy of the patients, their personal details were anonymized. Our ethics committee waived the requirement for informed consent for this study due to its retrospective nature and the fact that the data analysis was anonymous and confidential. Statistical analysis was conducted solely for academic purposes.

Clinical Data and Biochemical Indicators
Diabetes mellitus was defined as fasting blood glucose≥126 mg/dL or currently receiving antidiabetic medication therapy,[35] while hypertension was defined as systolic blood pressure≥140mmHg or diastolic blood pressure≥90mmHg, or receiving anti-hypertension treatment at present.[36] Dyslipidemia was defined as two or more of these four criteria: fasting serum triglyceride ≥1.70 mmol/L, TC≥5.20 mmol/L, LDL cholesterol ≥3.4 mmol/L, or HDL cholesterol≤ 0.91 mmol/L.[37]
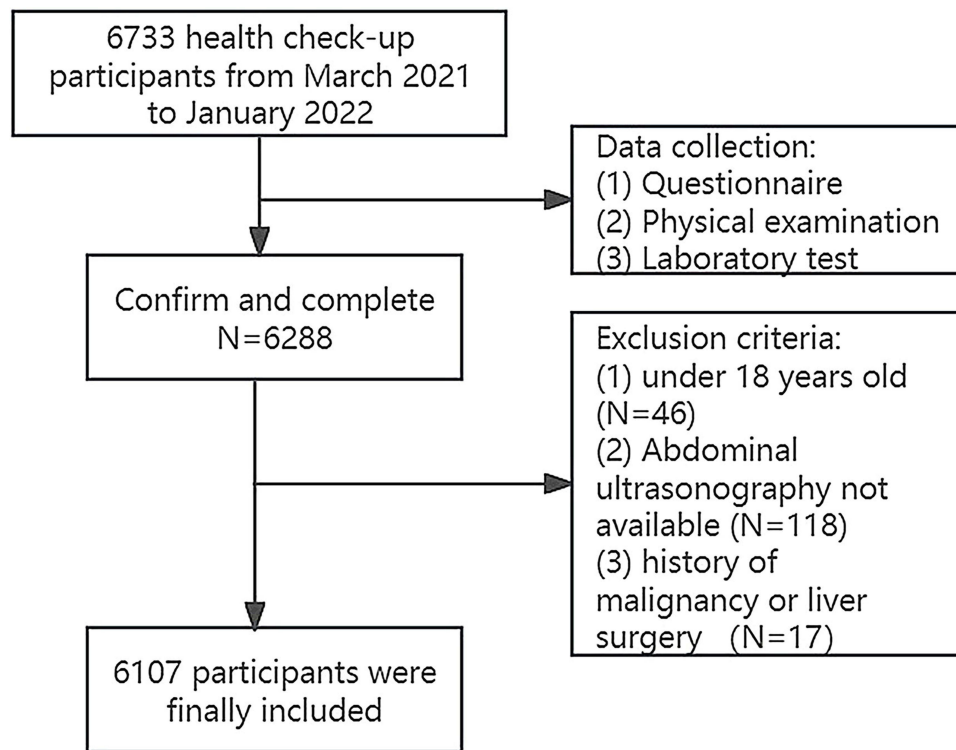
Figure 1 Flowchart of participants excluded and included in this study.

Blood samples (10–15mL) were taken from the antecubital vein of participants after a 12-hour fast. The serum was left at room temperature for 30 minutes and then centrifuged at 3000 rpm for 10 minutes. The serum was analyzed within 1 hour of collection to measure Fasting Plasma Glucose (FPG), Triglycerides (TG), Total Cholesterol (TC), Low-Density -Lipoprotein Cholesterol (LDL-C), High-Density-Lipoprotein Cholesterol (HDL-C), Serum Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), White Blood Cells (WBC), Neutrophils (NE) and Lymphocytes (LY). All blood samples were tested within 24 hours in the Medical Laboratory Center of Huadong sanatorium.

Assessment of CMI

To calculate the TG/HDL-C ratio, the serum concentration of TG (in mmol/L) was divided by HDL-C, and WHtR was computed by dividing WC (in cm) by height (in cm). The CMI was then obtained by multiplying TG/HDL-C and WHtR, as per the published formula.[27]

Definition of MAFLD

MAFLD was identified when hepatic steatosis was present, and at least one of the following criteria:[1] being overweight or obese (BMI≥23 kg/m^2), having type 2 diabetes mellitus, or exhibiting metabolic dysregulation. Metabolic dysregulation was defined by the occurrence of at least two of the following risks for metabolic disorders: ①waist circumference≥90/80 cm in Asian men and women; ②blood pressure ≥130/85 mmHg or specific drug treatment for controlling blood pressure; ③plasma triglyceride≥1.7 mmol/L or specific drug treatment; ④plasma high-density lipoprotein cholesterol < 1.0 mmol/L for men and < 1.3 mmol/L for women or specific drug treatment; ⑤prediabetes with fasting glucose levels between 5.6 to 6.9 mmol/L; ⑥homeostasis model assessment of insulin resistance (HOMA-IR) score ≥2.5; ⑦Plasma high sensitivity C-reactive protein (CRP) level >2 mg/L.

After 12 hours of fasting, abdominal high-resolution ultrasonography (SIMENS ACUSON S2000 ABVS) was used to measure hepatic steatosis. Experienced radiologists conducted the ultrasonography and identified the condition based on the following ultrasound images: diffusely increased near field echo of the liver ("bright liver"), a larger echo

of the liver than that of the kidney or spleen, vascular blurring, and poor visibility of the posterior right lobe due to deep attenuation.

Statistical Analysis

All statistical analyses were performed using SPSS 26.0 software and RStudio version 4.0.1. Continuous variables are reported as mean ± SD or median with interquartile range according to the evaluation of the normal distribution by the Kolmogorov–Smirnov test, and categorical variables are presented as the numbers(n) with percentages (%). Comparisons of baseline characteristics and laboratory parameters specified by gender among two groups were conducted using the Student's *t*-test or Mann–Whitney *U*-test for continuous variables, and the chi-square test for categorical variables as appropriate. Besides, the chi-square test or one-way ANOVA, or Kruskal–Wallis *H*-test were used for inter-group comparison stratified by CMI quartiles. Univariable correlations between variables were assessed using Pearson's correlation coefficients and presented by heatmap. A restricted cubic spline model was performed to estimate the association between CMI and MAFLD in a fully adjusted model. The knots were located at the 5th, 35th, 65th, and 95th percentiles. Additionally, a multivariable regression model was used to evaluate the relationship between CMI and MAFLD by gender, adjusting for potential confounders. Model 1 adjusted age, smoking, drinking, WC, BMI, WHtR, diabetes, hypertension and dyslipidemia. Model 2 adjusted Model 1 plus AST, ALT, WBC, NE and LY. Adjusted odds ratios (ORs) were presented with 95% confidence interval (CI). P for trend was evaluated for linear trend test using the median value of CMI as a continuous variable in the adjusted models. Receiver operating characteristic (ROC) curves were then generated to obtain the values of the area under the curve (AUC), with sensitivity, specificity, and 95% CI for each obesity-related indexes as a predictor of MAFLD. A two-tailed P-value <0.05 was considered statistically significant.

Results
Baseline Characteristics of Participants

In total, 6107 eligible participants were included in the study, comprising 3851 males and 2256 females (Table 1). 43.5% of males (1676/3851) and 16.2% of females (366/2256) were diagnosed with MAFLD. Subjects with MAFLD showed significantly higher age, waist circumference, BMI, WHtR, systolic and diastolic blood pressure, fasting blood glucose, triglycerides, total cholesterol, LDL-C, AST, ALT, WBC, NE, and LY, as well as a higher prevalence of diabetes, hypertension, and dyslipidemia, compared to non-MAFLD subjects (all P-values <0.001). In addition, MAFLD subjects in the male group had a significantly higher proportion of smokers than non-MAFLD subjects. Furthermore, MAFLD prevalence increased with increasing quartiles of CMI in both males and females (all P for trend <0.001) (Figure 2). Additionally, as shown in Table 2, regardless of sex, compared to subjects in the low quartile of CMI group, those in the high quartiles of CMI group had advanced age, increased waist circumference, BMI, WHtR, fasting blood glucose, triglycerides, AST, ALT, WBC, NE, and LY, with a greater proportion of diabetes, hypertension, and dyslipidemia (all P for trend <0.001). Moreover, males in the higher quartile of CMI had an increased proportion of current smokers and drinkers (P for trend <0.001), while HDL-C significantly decreased with the elevated quartile of CMI in females (P for trend = 0.017).

Correlation Analysis Between Baseline Variables and CMI

Pearson's correlation coefficients were used to assess the correlation between CMI and baseline variables, disregarding sex (Figure 3). All the baseline variables, except age, had a significant correlation with CMI, with HDL-C and LDL-C having a negative relationship and the other variables having a positive correlation (all P-value<0.001). Notably, TG had the strongest correlation with CMI, and can be considered as a reliable indicator in diagnosing MAFLD.

## Dose-Response Relationship Between CMI and MAFLD by Sex

Figure 4 displays the relationship between CMI and MAFLD risk in all participants. The horizontal line shows the 5th, 35th, 65th, and 95th percentiles of CMI, while the blue line represents the multivariable-adjusted ORs for MAFLD with

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Table 1 Baseline Characteristics of the Study Population According to Sex (n=6107)

Variables	Overall (n=6107)	Males (n=3851)		t, Z/χ²	P-value	Females (n=2256)		t, Z/χ²	P-value
		Non-MAFLD (n=2175)	MAFLD (n=1676)			Non-MAFLD (n=1890)	MAFLD (n=366)		
Age (years)	46.00 (37.00~55.00)	46.00 (36.00~55.00)	48.00 (40.00~56.00)	−5.08	<0.001	43.00 (34.75~52.00)	54.00 (45.00~60.00)	−12.78	<0.001
Smoking, n (%)	1594 (26.1)	796 (36.6)	792 (47.3)	44.37	<0.001	5(0.3)	1(0.3)	0.001	0.976
Drinking, n (%)	1023 (16.8)	541 (24.9)	463 (27.6)	3.72	0.054	15 (0.8)	4(1.1)	0.329	0.533
WC (cm)	82.65±9.55	73.79±6.66	83.52±7.30	31.85	<0.001	83.76±6.58	91.03±7.35	23.65	<0.001
BMI (kg/m²)	24.49±3.27	22.27±2.50	25.98±3.25	32.67	<0.001	24.17±2.44	27.10±2.97	20.70	<0.001
WHtR	0.49±0.05	0.49±0.04	0.53±0.05	30.71	<0.001	0.46±0.04	0.53±0.05	24.26	<0.001
CMI	0.50 (0.29~0.88)	0.48 (0.32~0.75)	0.99 (0.68~1.49)	−31.56	<0.001	0.26 (0.18~0.40)	0.65 (0.44~0.95)	−21.41	<0.001
SBP (mmHg)	122.00 (111.00~132.00)	123.00 (114.00~132.00)	129.00 (120.00~137.00)	−12.77	<0.001	112.00 (103.00~123.00)	123.50 (113.85~134.00)	−12.87	<0.001
DBP (mmHg)	73.00 (66.00~80.00)	73.00 (67.00~80.00)	78.00 (71.00~85.00)	−14.90	<0.001	69.00 (62.00~75.00)	73.00 (68.00~82.00)	−9.83	<0.001
Hypertension, n (%)	777 (12.7)	238 (10.9)	351 (20.9)	73.07	<0.001	122 (6.5)	66 (18.0)	53.81	<0.001
Dyslipidemia, n (%)	2517 (41.2)	803 (36.9)	993 (59.2)	189.63	<0.001	544 (28.8)	177 (48.4)	54.05	<0.001
Diabetes, n (%)	388 (6.4)	91 (4.2)	226 (13.5)	108.40	<0.001	24 (1.3)	47 (12.8)	134.70	<0.001
FBG (mmol/L)	5.20 (4.91~5.60)	5.18 (4.92~5.54)	5.47 (5.12~6.09)	−16.03	<0.001	5.00 (4.76~5.27)	5.47 (5.14~6.02)	−15.59	<0.001
TG (mmol/L)	1.28 (0.89~1.92)	1.23 (0.92~1.72)	2.00 (1.46~2.76)	−27.52	<0.001	0.89 (0.69~1.20)	1.54 (1.16~2.10)	−19.28	<0.001
TC (mmol/L)	4.83 (4.27~5.40)	4.78 (4.24~5.32)	4.93 (4.37~5.52)	−5.52	<0.001	4.78 (4.22~5.36)	4.95 (4.44~5.59)	−4.03	<0.001
HDL-C (mmol/L)	1.26 (1.07~1.52)	1.25 (1.09~1.45)	1.06 (0.92~1.21)	−23.49	<0.001	1.54 (1.32~1.78)	1.25 (1.09~1.45)	−14.65	<0.001
LDL-C (mmol/L)	3.11 (2.60~3.61)	3.13 (2.64~3.61)	3.21 (2.67~3.74)	−3.37	<0.001	2.96 (2.48~3.49)	3.23 (2.68~3.73)	−5.21	<0.001
ALT (IU/L)	18.00 (13.00~27.00)	18.00 (14.00~24.00)	28.00 (20.00~41.00)	−26.20	<0.001	13.00 (10.00~17.00)	22.00 (16.00~31.25)	−18.13	<0.001
AST (IU/L)	17.00 (14.00~21.00)	17.00 (14.10~20.00)	20.00 (16.00~25.00)	−15.97	<0.001	15.00 (13.00~18.00)	18.00 (15.00~23.00)	−9.48	<0.001
WBC (×10⁹/L)	6.05 (5.14~7.04)	6.09 (5.18~7.00)	6.63 (5.75~7.64)	−12.24	<0.001	5.48 (4.69~6.45)	6.10 (5.27~7.08)	−7.65	<0.001
NE (×10⁹/L)	3.27 (2.66~4.00)	3.24 (2.66~3.93)	3.61 (2.97~4.33)	−10.96	<0.001	3.01 (2.43~3.69)	3.36 (2.71~4.08)	−5.90	<0.001
LY (×10⁹/L)	2.15 (1.80~2.56)	2.17 (1.84~2.56)	2.33 (1.95~2.77)	−8.14	<0.001	1.98 (1.64~2.34)	2.20 (1.87~2.52)	−6.87	<0.001

Notes: Data are presented as mean with standard deviation, median with the interquartile range [M (P25-P75)], or numbers (percentage) [n (%)] as appropriate. Comparison of the differences between the two groups were examined by Student's *t*-test, Mann–Whitney *U*-test or chi-square test, respectively.
Abbreviations: CMI, cardiometabolic index; MAFLD, metabolic dysfunction-associated fatty liver disease; WC, waist circumference; BMI, body mass index; WHtR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell; NE, neutrophil; LY, lymphocyte.
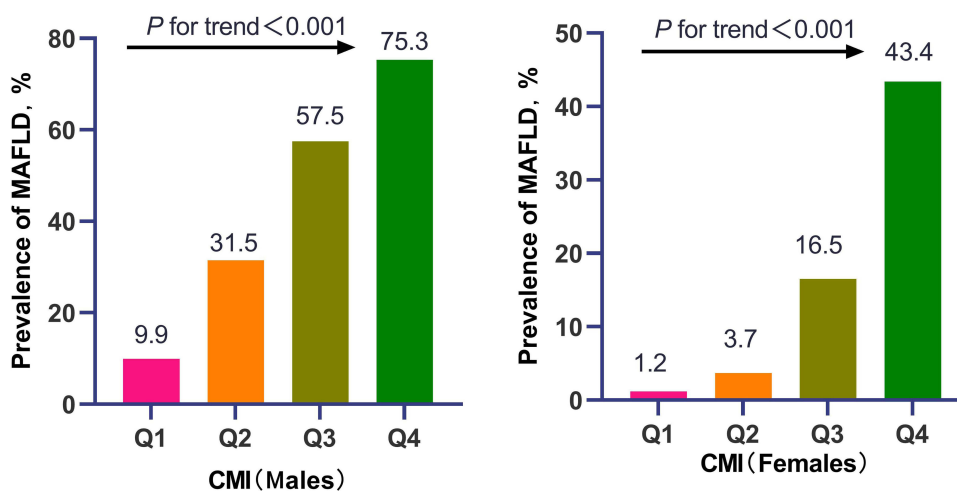
Figure 2 Prevalence of MAFLD according to CMI quartile by sex.
Abbreviations: MAFLD, metabolic associated fatty liver disease; CMI, cardiometabolic index.

knots located at the 5th, 35th, 65th, and 95th percentiles of CMI. Analysis showed a non-linear correlation between CMI and MAFLD risk (all P for non-linearity < 0.001). Multivariable adjusted restricted cubic spline analysis revealed that increased CMI values significantly increased MAFLD risk when CMI was above its median.

Multivariate Logistic Regression Assessing CMI on the Risk of MAFLD

In multivariate logistic regression analyses, CMI expressed as either continuous variables or quartiles, significantly associated with MAFLD in all models (Table 3). After adjusting for potential confounding factors, the ORs (95% CI) for per SD increase of CMI were 2.72 (2.35–3.15) for males and 3.26 (2.36–4.51) for females (all P-value<0.001). Upon dividing CMI into quartiles, its association with MAFLD risk remained statistically significant, subjects in the highest quartile of CMI exhibited a 15.82-fold (95% CI:11.84–21.14) MAFLD risk in males and 22.60-fold (95% CI:9.52–53.65) MAFLD risk in females. Furthermore, all participants tended to have increased odds of developing MAFLD with an elevated quartile of CMI (all P for trend<0.001).

Diagnostic Capacity of Obesity-Related Indices and TG in Predicting MAFLD

The ROC curves and optimal cutoff points of obesity-related indices and TG were plotted in Figure 5 and Table 4 to predict MAFLD based on sex. In males, the highest AUC was displayed by CMI (0.796, 95% CI: 0.782–0.810), followed by WC (0.770, 95% CI: 0.756–0.785), BMI (0.778, 95% CI: 0.763–0.792), TG (0.758, 95% CI: 0.743–0.773), and WHtR (0.758, 95% CI: 0.743–0.773). Similarly, in females, CMI had the highest AUC (0.853, 95% CI: 0.834–0.872), followed by WC (0.841, 95% CI: 0.821–0.861), BMI (0.830, 95% CI: 0.808–0.853), TG (0.818, 95% CI: 0.796–0.840), and WHtR (0.830, 95% CI: 0.808–0.851). It is noteworthy that, in both sexes, CMI was more accurate than other obesity-related indexes and TG in distinguishing MAFLD

Discussion

This retrospective study based on the general population aimed to explore the relationship between CMI and MAFLD in both sexes. The results of the multivariate regression analysis revealed that individuals with high CMI had a significantly increased risk of MAFLD. Moreover, CMI was found to be the most reliable predictor of MAFLD in both sexes, compared to obesity-related indicators and TG.

Recent research has indicated that MAFLD, a 2020 redefinition of NAFLD, is more than just a name change.[38] Our study found that the metabolic indicators, such as serum FBG, HDL-C, LDL-C, TC, TG, ALT, AST and CMI, of subjects in the MAFLD group were higher than those in the control group. A separate study of adults over 40 years old with MAFLD revealed that metabolic disorders were more pronounced.[39] It is believed that hepatic steatosis, a systemic

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**Table 2** Baseline Characteristics of the Study Population by CMI Quartiles According to Sex (n=6107)

Characteristics	Male (n=3851)				P-value	P for Trend	Female (n=2256)				P-value	P for Trend
	Q1 (n=963) (0.08~0.41)	Q2 (n=963) (0.42~0.67)	Q3 (n=963) (0.68~1.09)	Q4 (n=963) (1.10~17.23)			Q1 (n=564) (0.06~0.19)	Q2 (n=564) (0.20~0.30)	Q3 (n=564) (0.31~0.49)	Q4 (n=564) (0.50~11.33)		
Age (years)	39.00 (32.00~46.00)	42.00 (35.00~52.00)	47.00 (39.00~57.00)	51.50 (42.00~58.00)	<0.001	<0.001	44.00 (35.00~56.00)	47.00 (38.00~56.00)	47.00 (39.00~56.25)	47.00 (40.00~55.00)	<0.001	<0.001
Smoking, n (%)	280 (29.1)	363 (37.7)	428 (44.5)	517 (53.7)	<0.001	<0.001	1(0.2)	0(0)	3(0.5)	2(0.4)	<0.001	0.273
Drinking, n (%)	198 (20.6)	248 (25.8)	244 (25.4)	314 (32.6)	<0.001	<0.001	4(0.7)	4(0.7)	6(1.1)	5(0.9)	<0.001	0.607
WC (cm)	81.65±6.56	86.15±6.59	88.53±6.91	91.36±7.69	<0.001	<0.001	70.24±5.90	73.29±5.82	77.02±6.56	80.93±7.68	<0.001	<0.001
BMI (kg/m^2)	23.57±2.49	25.07±2.55	25.92±2.77	27.21±3.15	<0.001	<0.001	21.07±2.12	22.17±2.23	23.38±2.74	24.87±3.23	<0.001	<0.001
WHtR	0.47±0.04	0.50±0.04	0.52±0.04	0.53±0.05	<0.001	<0.001	0.44±0.04	0.46±0.04	0.48±0.04	0.51±0.05	<0.001	<0.001
Hypertension, n (%)	91 (9.4)	136 (14.1)	152 (15.8)	210 (21.8)	<0.001	<0.001	10 (1.8)	34 (6.0)	61 (10.8)	83 (14.7)	<0.001	<0.001
Diabetes, n (%)	40 (4.2)	60 (6.2)	88 (9.1)	129 (13.4)	<0.001	<0.001	3(0.5)	6(1.1)	18 (3.2)	44 (7.8)	<0.001	<0.001
FBG (mmol/L)	5.15 (4.87~5.49)	5.26 (4.97~5.63)	5.36 (5.04~5.85)	5.46 (5.10~6.07)	<0.001	<0.001	4.85 (4.65~5.11)	5.00 (4.76~5.25)	5.11 (4.86~5.42)	5.30 (4.98~5.76)	<0.001	<0.001
TG (mmol/L)	0.87 (0.73~1.01)	1.28 (1.13~1.47)	1.81 (1.59~2.04)	2.98 (2.42~3.92)	<0.001	<0.001	0.61 (0.52~0.69)	0.83 (0.75~0.93)	1.11 (0.98~1.26)	1.73 (1.47~2.22)	<0.001	0.013
TC (mmol/L)	4.61 (4.10~5.16)	4.85 (4.29~5.36)	4.88 (4.32~5.44)	5.04 (4.48~5.68)	<0.001	0.369	4.70 (4.17~5.24)	4.70 (4.16~5.21)	4.84 (4.26~5.41)	5.00 (4.45~5.64)	<0.001	0.100
HDL-C (mmol/L)	1.45 (1.29~1.64)	1.22 (1.11~1.34)	1.09 (0.99~1.20)	0.95 (0.84~1.06)	<0.001	0.159	1.85 (1.66~2.04)	1.57 (1.43~1.75)	1.41 (1.27~1.55)	1.17 (1.04~1.32)	<0.001	0.017
LDL-C (mmol/L)	2.96 (2.49~3.45)	3.28 (2.80~3.74)	3.31 (2.86~3.82)	3.10 (2.50~3.64)	<0.001	0.005	2.66 (2.29~3.18)	2.93 (2.48~3.41)	3.14 (2.66~3.65)	3.26 (2.70~3.74)	<0.001	0.018
Dyslipidemia, n (%)	222 (23.1)	318 (33.0)	490 (50.9)	766 (79.5)	<0.001	<0.001	114 (20.2)	134 (23.8)	184 (32.6)	289 (51.2)	<0.001	<0.001
ALT (IU/L)	17.00 (13.00~23.00)	20.00 (15.00~28.00)	24.00 (17.00~34.00)	28.00 (20.00~41.00)	<0.001	<0.001	11.00 (9.00~15.00)	13.00 (10.00~17.00)	14.00 (11.00~19.00)	18.00 (13.00~27.00)	<0.001	<0.001
AST (IU/L)	17.00 (15.00~20.00)	18.00 (15.00~21.00)	18.00 (15.00~22.00)	20.00 (16.00~26.00)	<0.001	<0.001	15.00 (13.00~18.00)	15.00 (13.00~18.00)	16.00 (13.00~19.00)	17.00 (14.00~21.00)	<0.001	<0.001
WBC (×10^9/L)	5.78 (5.01~6.61)	6.24 (5.42~7.15)	6.51 (5.56~7.45)	6.80 (5.83~7.96)	<0.001	<0.001	5.24 (4.51~6.17)	5.49 (4.75~6.52)	5.66 (4.82~6.56)	6.00 (5.08~6.94)	<0.001	<0.001
NE (×10^9/L)	3.09 (2.52~3.70)	3.32 (2.78~4.05)	3.51 (2.89~4.19)	3.70 (3.01~4.46)	<0.001	<0.001	2.86 (2.31~3.51)	3.05 (2.45~3.70)	3.13 (2.59~3.82)	3.24 (2.59~4.01)	<0.001	<0.001
LY (×10^9/L)	2.11 (1.79~2.47)	2.21 (1.87~2.61)	2.28 (1.92~2.69)	2.37 (1.99~2.87)	<0.001	<0.001	1.91 (1.59~2.26)	1.97 (1.62~2.34)	2.02 (1.70~2.38)	2.15 (1.84~2.53)	<0.001	<0.001

Notes: Continuous data are presented as mean with standard deviation or median with the interquartile range [M (P25-P75)], and categorical data as frequency (percentage) [n (%)]. Comparison of the differences among groups were examined by ANOVA, Kruskal–Wallis *H*-test or chi-square test according to the type and distribution pattern of variables.
Abbreviations: CMI, cardiometabolic index; WC, waist circumference; BMI, body mass index; WHtR, waist-to-height ratio; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell; NE, neutrophil; LY, lymphocyte.
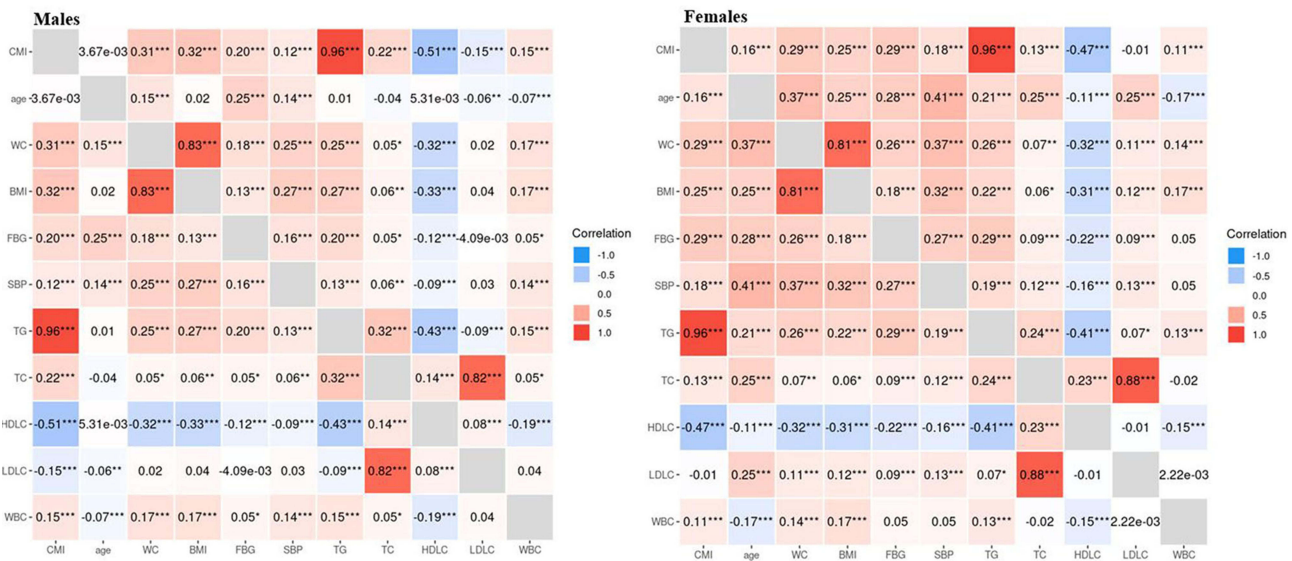
Figure 3 The heatmap of the correlation between baseline variables and CMI using the Pearson's correlation analysis among by sex. *$P<0.05$;**$P<0.01$;***$P<0.001$.
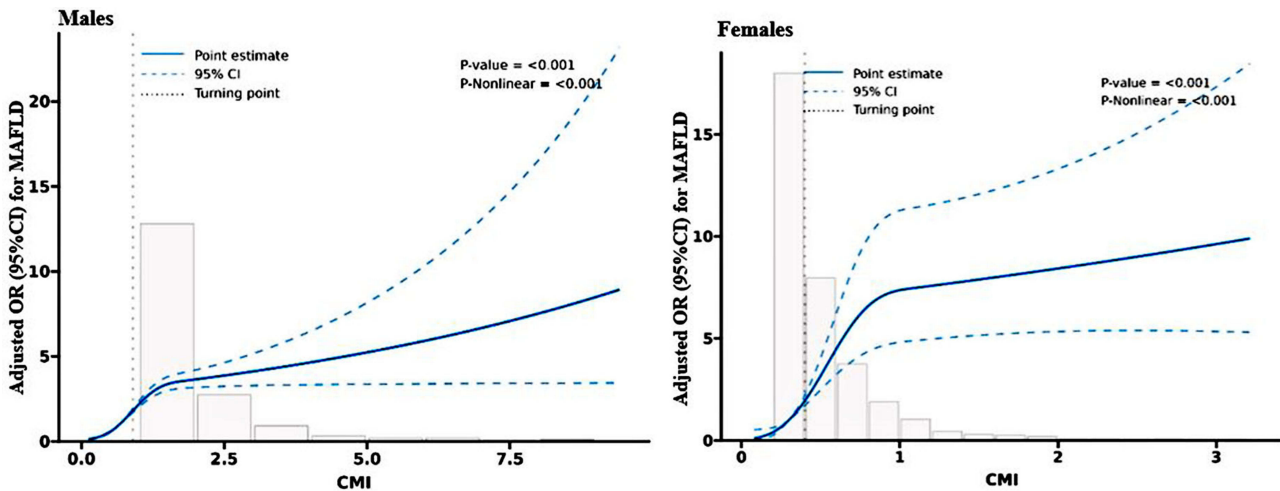
Figure 4 Restricted cubic spline of the association between CMI and MAFLD risk by sex. The association was adjusted for age, smoking, drinking, WC, BMI, WHtR, diabetes, hypertension, dyslipidemia, AST, ALT, WBC, NE and LY. The medians CMI of males (0.9) and females (0.4) were chosen as a reference. The plot showed an increased risk of MAFLD with the elevated CMI, which were above the medians of CMI.
Abbreviations: OR, odds ratio; CI, confidence intervals.

metabolic disorder, is caused by increased lipid acquisition and/or decreased lipid metabolism.[40] This leads to lipids being transported to various organs of the body, resulting in visceral obesity and abnormalities in various metabolic-related indicators.[41]

A recent cross-sectional study involving 3239 females investigated the association between various blood lipid-related indexes in predicting NAFLD. The results showed that the area under the curve (AUC) of CMI was significantly higher than the other indexes, including triglyceride glucose index (TyG), TG/HDL-C, TC/HDL-C, and LDL-C/HDL-C. This suggests that CMI could be a recommended index in the screening of NAFLD in women, as it is useful for detecting populations that are at high risk of NAFLD.[34] Additionally, another study explored the association of lipid accumulation product (LAP) and CMI with the NAFLD risk, and found that these indexes are convenient for the screening and quantification of NAFLD among Chinese adults, with a greater association with NAFLD in women than in men.[33]

Table 3 Adjusted Associations Between CMI Quartiles and MAFLD Risk by Gender

Variables	Odds Ratio (95% CI)					
	Crude	**P-value**	**Model 1**	**P-value**	**Model 2**	**P-value**
Males						
CMI (Per SD increase)	4.34 (3.78–4.98)	<0.001	3.71 (3.19–4.30)	<0.001	2.72 (2.35–3.15)	<0.001
CMI (Quartile)						
1th quartile	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
2th quartile	4.19 (3.26–5.40)	<0.001	4.06 (3.14–5.23)	<0.001	3.22 (2.47–4.20)	<0.001
3th quartile	12.35 (9.65–15.82)	<0.001	11.62 (9.01–14.99)	<0.001	8.35 (6.40–10.89)	<0.001
4st quartile	27.83 (21.51–36.01)	<0.001	24.70 (18.72–32.58)	<0.001	15.82 (11.84–21.14)	<0.001
P for trend	<0.001		<0.001		<0.001	
Females						
CMI (Per SD increase)	9.52 (6.88–13.17)	<0.001	6.09 (4.36–8.50)	<0.001	3.26 (2.36–4.51)	<0.001
CMI (Quartile)						
1th quartile	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
2th quartile	3.08 (1.30–7.30)	0.011	2.58 (1.08–6.16)	<0.001	2.46 (0.95–6.37)	0.063
3th quartile	15.71 (7.22–34.20)	<0.001	10.94 (4.97–24.08)	<0.001	9.04 (3.77–21.69)	<0.001
4st quartile	61.11 (28.47–131.17)	<0.001	39.19 (18.05–85.10)	<0.001	22.60 (9.52–53.65)	<0.001
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: adjusted for age, smoking, drinking, WC, BMI, WHtR, diabetes, hypertension and dyslipidemia. Model 2: adjusted for Model 1 plus AST, ALT, WBC, NE and LY.

Our study found that a higher CMI quartile was markedly and independently correlated with an enhanced MAFLD risk in both males and females. The CMI, a newly developed index based on TG/HDL-C and WHtR values,[27] has been related to obesity-related metabolic diseases such as cardiovascular disease and chronic conditions like diabetes and
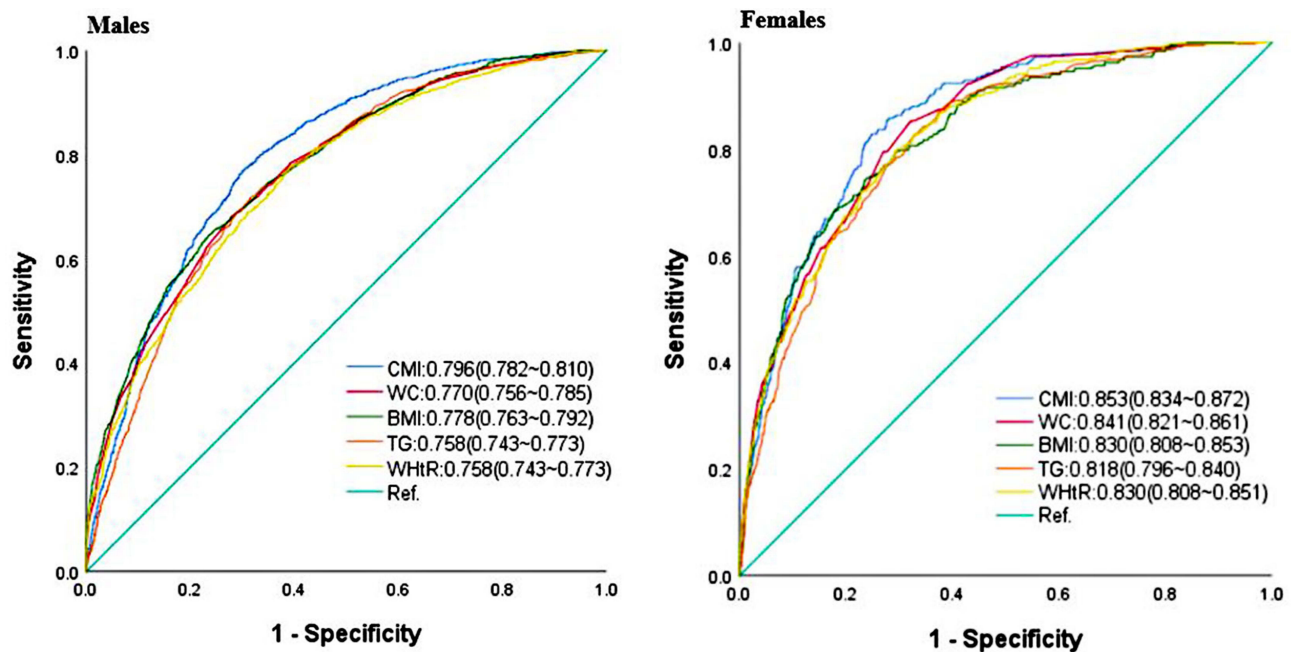
Figure 5 ROC curve comparison of obesity-related indices and TG in predicting MAFLD by sex.

Table 4 AUCs of Various Indexes for Discriminating MAFLD by Sex

Variables	AUC (95% CI)	Cut-Off Value	Sensitivity (%)	Specificity (%)	P-value
Males					
CMI	0.796 (0.782–0.810)	0.86	76.9	69.9	<0.001
BMI (kg/m^2)	0.770 (0.756–0.785)	25.85	64.5	76.5	<0.001
WC (cm)	0.778 (0.763–0.792)	87.71	67.3	72.6	<0.001
WHtR	0.758 (0.743–0.773)	0.50	77.6	70.9	<0.001
TG (mmol/L)	0.758 (0.743–0.773)	1.55	72.0	68.1	<0.001
Females					
CMI	0.853 (0.834–0.872)	0.41	82.8	75.2	<0.001
BMI (kg/m^2)	0.841 (0.821–0.861)	23.86	74.6	76.1	<0.001
WC (cm)	0.830 (0.808–0.852)	76.76	85.2	67.9	<0.001
WHtR	0.830 (0.808–0.851)	0.48	79.8	70.5	<0.001
TG (mmol/L)	0.818 (0.796–0.840)	1.05	84.2	65.6	<0.001

hypertension.[30,31] WHtR is a measure of abdominal obesity that is associated with lipid content and distribution, and is more effective than WC and BMI in evaluating fatty liver disease.[42] Studies have also shown that TG/HDL-C is closely related to insulin resistance, obesity, and metabolic disorders, and can be used to predict NAFLD.[20,43,44] Abdominal obesity can lead to high levels of glucose and lipid oxidation, resulting in an accumulation of fatty acids in the liver.[45,46] Insulin resistance can also increase the secretion of VLDL and TG, while reducing HDL-C levels.[47,48] Furthermore, insulin resistance can promote the development of NAFLD by decomposing TG in adipose tissue and enhancing TG synthesis in the liver.[49,50] ROC analyses have indicated that CMI has a satisfactory diagnostic performance.

The ROC analysis showed that CMI was more effective in identifying MAFLD among females than males. This is in line with a study in China that suggested CMI as a reliable indicator for screening women for NAFLD.[34] It is reasonable to assume that CMI's performance may be affected by age, as metabolism, body composition, and coexisting diseases change with age.[51–53] As for gender differences, this may be due to the difference in fatty acid accumulation and metabolism, as females tend to have more visceral lipolysis and fatty acid delivery to visceral fat than males.[54] Additionally, the different hormones between the sexes may affect fat distribution, which in turn affects the relationship between CMI and MAFLD.[55]

This study had several noteworthy limitations. This single-center study and cross-sectional design only enabled us to observe the correlation between CMI and MAFLD; consequently, longitudinal studies in multiple centers are essential to explore the causal relationship. Additionally, as the participants were recruited from a health check-up population in China, these findings may not be applicable to other racial or ethnic groups. Furthermore, due to the lack of parameters necessary to calculate the score of liver fibrosis, it was not possible to analyze the relationship between CMI and fibrosis. Lastly, even though the current study took measures to identify confounders, there may still be residual unmeasurable or unreported confounding variables, such as diet patterns and regular exercise.

Conclusion

This study delved into the correlation between CMI and MALFD and established that CMI had a superior predictive power for MAFLD, particularly in females. Moreover, the best cutoff values of CMI for predicting MAFLD in both genders were determined and demonstrated excellent diagnostic accuracy for MALFD. CMI, which is composed of traditional blood lipid indexes and anthropometric indexes, is advantageous as it is easy to obtain, inexpensive, and has high diagnostic accuracy. Therefore, CMI is clinically beneficial for early identification of MAFLD and is worthy of clinical utilization.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author (Baiqing Xu, Email: doctorxbq@163.com) upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no potential competing interests in this work.

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